

# Acute Abdomen During Pregnancy

Goran Augustin

*Third Edition*



WORLD SOCIETY OF  
EMERGENCY SURGERY



 Springer

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Third Edition

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*To my father, an abdominal surgeon whose ability to make an accurate diagnosis of emergency abdominal condition only with history taking and physical examination was never outperformed. He taught me great things in this “clinical magic.”*

*To my wife Katarina, despite having two small children, understood the importance of this work to me and sacrificed almost a decade of many weekends, evenings, nights, and journeys to allow me and provide me enough time to create both the first and the second edition of this book.*

*To my children (Lara and Lukas), who remind me every day that teaching others is a great opportunity and pleasure that cannot be substituted.*

*To my mother, whose mathematically functioning brain is fascinating, and now I realize that it is a fortune that I inherited most parts of it.*

*And... to all pregnant women... who are healthy... and to all who need the clinicians' consultations from this book, whose lives and lives of their future babies will be saved and normal....*

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## Foreword I to the Second Edition

Diagnosis and treatment of abdominal surgical emergencies during pregnancy are challenging. Abdominal examination is difficult, and organs may be pushed by the uterus in relation to gestation age, obscuring abdominal pathologies. Physiological parameters are altered due to pregnancy-induced changes, and laboratory tests could be deranged due to pregnancy-induced variations. In evaluating abdominal emergencies in gravid women, the physician is advised to use computed tomography for diagnosis. Radiation exposure may affect the fetus's normal development. Indeed a perplexing clinical setup.

Delay in the diagnosis of surgical emergencies is associated with the amplified risk to the mother and the fetus. The need for nonobstetrical surgery during pregnancy is low. However, nonobstetric surgery is fraught with increased risk to the fetus. Fortunately, in most cases, the gravid woman is a young and healthy individual, and the surgical emergencies are confined to young patients. The gestational risk in pregnant women with an acute abdomen is multifactorial. Some relate to the patient and her well-being, and some relate to the fetal age of gestation at the time of diagnosis. Peritonitis and sepsis contribute to the risks, and the surgical approach (laparoscopic vs. open) has a great deal of impact.

Dr. Goran Augustin has assembled data on surgical emergencies in pregnant women and wisely outlined recommendations for the practicing surgeon faced with a gravid patient endangered with an abdominal surgical emergency.

Any surgery during pregnancy confers significant obstetrical risk. Delaying investigation and diagnosis may render the patient and her fetus to worse

outcomes. Surgeons should be aware of pregnancy physiology and the precise algorithm for diagnosis and management during gestation. This book offers exactly that.

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## Foreword II to the Second Edition

I have been invested with the honor (and responsibility) of writing a “FORE” “WORD” meaning to write thoughtful comments made about a book, to give the impression as to what this book is all about. Acute abdomen during pregnancy is a dramatic event, with significant morbidity and mortality for both mother and fetus. Despite this, acute abdomen during pregnancy does remain a neglected and not well-known topic.

Clearly, a pregnant patient presenting with an acute abdomen is a clinical scenario that overlaps specialties. Common sense suggests the early involvement of specialists such as a surgeon, obstetrician/gynecologist, and a specialist in maternal-fetal medicine when dealing with this challenging situation.

Unfortunately, the diagnosis and treatment often tend to be delayed due to the peculiar physiological features of pregnancy and the restrictions imposed on diagnostic imaging techniques such as X-ray and CT due to the fear of radiation exposure. MRI is gaining an increasingly relevant role in the diagnostic workup but is not always and everywhere available or easily and readily accessible. Nevertheless, acute abdomen needs to be diagnosed in the shortest time possible and promptly treated. Physicians should pay attention in this regard as any delay may seriously deteriorate the condition of both mother and fetus.

The editor, Dr. Goran Augustin, is an internationally recognized expert in the field of the acute abdomen during pregnancy and given his research and clinical activity over the last decade, I can wholeheartedly state that he is now considered an internationally recognized expert in the management of acute appendicitis and other acute surgical diseases in pregnant patients. His dedication to this critical subset of patients has to be commended, and Dr. Augustin has made this delicate issue become his area of clinical practice and his field of scientific research throughout the years. Textbooks and surgical journals appear to be the written resource of the fundamentals and the research reporting archives of the knowledge and the craft of this surgical discipline. This textbook is one of those resources and represents a landmark textbook in the field of the care of a pregnant patient. Both the trainee and the practitioner of acute care surgery but also gynecology and obstetrics as well as emergency physicians and family doctors will find this textbook useful and a ready resource for current approaches to surgical emergencies.

This will soon be a standard text used by surgeons who practice Acute Care Surgery worldwide and any physician dealing with critical surgical care during pregnancy. It has been a privilege to review it.

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## Preface to the Third Edition

*Only those who know the past & present of science and art will boost their progress with awareness.* (Christian Albert Theodor Billroth)

*Times are bad. Children no longer obey their parents, and everyone is writing a book.* (Marcus Tullius Cicero)

As Theodor Billroth said, I know the past and present of this book. That is how I know it should be improved in every way. And that is the future of this book. To be better. To give a reader new insights into every detail of the acute abdomen during pregnancy. That is why the third edition is in front of us. The knowledge about these rare entities expands with every new case treated and every new article or case report on the subject published. As always, new knowledge opens new questions and new dilemmas. During writing this third edition again, I recall Marvin Corman's Preface to the sixth edition of *Colon and Rectal Surgery* (see Preface for the second edition). Probably I will recall him with every new edition.

This new edition has been almost completely rewritten. For example, completely new chapters include *Bariatric Surgery*, *Fetal Trauma*, *Vernix Caseosa Peritonitis*, and *Radiology*. Interestingly, I could not find these chapters in any book. Dealing with pregnant patients after bariatric surgery is extremely important due to the increasing frequency of these procedures in the general population. The important finding is that plain abdominal X-ray is frequently normal, delaying accurate diagnosis and surgical treatment. All this can have deleterious consequences on the mother and fetus. The chapter dealing with intrauterine fetal trauma is also important. It adds the knowledge on intrauterine injuries with their influence on the timing and type of delivery. The chapter on vernix caseosa peritonitis is very interesting because surgeons never consider this condition a cause of postdelivery complications. Accurate diagnosis can sometimes avoid unnecessary operations or organ resections due to the suspicion of a cause of peritonitis or even an underlying tumor. The chapter *Urologic emergencies* from the previous edition was divided into three chapters which are expanded and updated: *Complicated Urinary Tract Infections*, *Urinary Tract Obstruction*, and *Urinary Tract Bleeding*. The text is significantly expanded and reorganized. It is published in two volumes for easier handling and reading. Many procedures are written in more detail with additional photographs to help in their comprehension.

It is difficult to construct data-based guidelines on these rare occurrences. Even a rarer occurrence is the detection of intrauterine fetal injuries. Should



we deliver a viable fetus with dislocated fracture of long bones? Should delivery always be by Cesarean section to minimize further movements of the bone fragments? What about fractures that look partly healed, especially in significant misalignment? We do not have prospective studies and long-term follow-ups. We should mostly rely on the biology and recommendations from neonates and infants. However, is this enough for excellent outcomes? Maybe this new edition would not give all the answers, but it could open our eyes and minds to think more profoundly about these sporadic cases in our clinical practice.

I express my gratitude to Donatella Rizza and the staff at Springer, who have supported the project from the beginning and helped bring this book to fruition. Therefore, I hope that Cicero was not right about my book. I hope that the reader will enjoy reading it!

Zagreb, Croatia

Goran Augustin

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## Preface to the Second Edition

*He who combines the knowledge of physiology and surgery, in addition to the artistic side of his subject, reaches the highest ideal in medicine.* (Christian Albert Theodor Billroth)

*I am fortunate again to have the opportunity of changing my mind, of clarifying confusion and my confused thinking, of correcting misstatements, as well as attempting to remain contemporary. I am doomed to the embarrassment of living with my previous inaccuracies. Still, it is better to recant than to be accused of having a pertinacious little mind.* (Marvin Corman (Preface to the sixth edition of *Colon and Rectal Surgery*))

*If a man will begin with certainties, he shall end in doubts; but if he will be content to begin with doubts, he shall end in certainties.* (Sir Francis Bacon)

When I started writing the first edition of this book, I read the foreword of one book, from an author whom I do not remember, where he wrote that he did not know that it was more difficult and more time-consuming to write the second edition of the same book. At first, I was surprised because I thought one could change several figures, add a little new text, and complete the new edition. I recalled the author's words and statements when I started improving the first edition. It is the whole truth! I was surprised when, several months after the first edition was published, I started to read my book again. I was surprised how many misinterpretations, errors, or scientific and clinical "gaps" were present. I was ashamed of how incomplete and inconsistent the book I wrote was. At the same time, I started to read the new sixth edition of Marvin Corman's book—*Colon and Rectal Surgery*. Before going to the specific topics that interested me, I read the Preface. And I was thrilled, relaxed, satisfied, and fulfilled at the same time. The citation that I took from Corman's *Preface* is true. Then, it was easier to finish this second edition, knowing it would be better than the first edition (and probably worse than future editions). Every chapter is expanded and updated, and four new chapters are added. The chapter on urologic emergencies helps to differentiate conditions that usually do not require operative interventions. Perioperative and anesthetic considerations, part of every chapter in the first edition, are concentrated in a separate chapter and significantly expanded. Many of these considerations are the same for the most acute abdominal conditions during pregnancy. One of the added chapters is especially interesting. It is about increased intra-abdominal pressure during pregnancy. This issue is complex, even in the general population. In pregnancy, it has additional difficulty

during the diagnostic workup and selecting appropriate treatment strategies for both the mother and the fetus.

My father, also an abdominal surgeon, watched me while writing the second edition for 2 years, day by day. Once, he came to me, knowing that I am the sole editor and author, and said: “*This book is concentrated energy, so much energy that could fill an atomic bomb.*” I can confirm that his statement is true when the text is completed. Concentrated energy or concentrated knowledge is what I want to share with every reader!

And now I repeat my plea from the Preface of the first edition. Contact me for any errors, misinterpretations, or medical/surgical mistakes in the text because I would like to improve (further editions of) this interesting subject. Dear authors, publish cases of the acute abdomen during pregnancy and publish comprehensive reviews so that the medical community could have a better insight into the incidence, etiology, diagnosis, treatment, and maternal and fetal outcome for all causes of the acute abdomen during pregnancy. Dear reviewers and editors of medical journals, please be sensitive to these important topics. Who knows, maybe, one day, a journal, for example, *Journal of Abdominal Surgery in Pregnancy* or *Digestive Diseases in Pregnancy*, will be created.

Zagreb, Croatia

Goran Augustin

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## Preface to the First Edition

*The art and science of asking questions is the source of all knowledge. (Thomas Berger)*

*What has given me the most joy in my life is the establishment of a school that carries on my aspirations and aims, be it scientific or humanitarian thereby ensuring a legacy for the future. (Theodor Billroth, 1893)*

*Earlier diagnosis means better prognosis. (Zachary Cope, 1921)*

How did the idea for the book come? Here is the answer. Acute abdomen is still one of the most exciting conditions in (emergency) surgery and medicine. The clinician needs to make the diagnosis and the indication for the operation as fast as possible. Then the operator should operate with the lowest possible morbidity and mortality. This has been known for over a century. Another difficulty arises when that clinician has a pregnant patient with an acute abdomen. Now they are dealing with two human beings at the same time. Also, the pregnant patient has slightly changed intraperitoneal anatomy and physiology, making the diagnosis more difficult.

During the last 7 years, I started to study more on the causes of acute abdomen during pregnancy. Searching through the literature, I found very few reviews on the subject. Unfortunately, that was expected because acute abdomen during pregnancy is a rare group of conditions. After excluding the most common causes, such as acute appendicitis and acute cholecystitis, the clinician will deal with other pathologies during pregnancy once in several years, sometimes once in a career. When I comprehended that, I started to study, write, and publish articles about different topics of the acute abdomen during pregnancy. When I tried to find some texts covering the whole topic, I could not find these. Then it came to me that I needed to write a book about *Acute Abdomen During Pregnancy*, first to help myself and then to help other clinicians dealing with this rare subject. Interestingly, some names in medicine, gynecology, and surgery that are not so famous or known were the first to treat such cases in medical history. It was interesting for me to read about them and to put them in the book. Mostly, these persons were more famous for other achievements in their medical fields.

There are two problems in writing a book that should have guidelines and recommendations on the topics included. First, it is the (extreme) rarity of these conditions. Second, the acute onset is unpredictable in the severity and the time of presentation. These facts preclude the possibility of randomized studies needed for validated guidelines and recommendations in medicine.

Therefore, some of the recommendations in the book are not adequately validated. Still, due to the rarity (some diseases have less than 50–100 cases published in 100 years), I tried to combine the recommendations from the acute abdomen in the general population and from the opinions of the authors (and myself) of published case reports. Therefore, many facts from these case reports are copied into this textbook. Also, the comprehensiveness of the chapters is not equal and mostly depends on the frequency of specific conditions during pregnancy. Hence, the most extensive chapters include acute appendicitis, acute cholecystitis, intestinal obstruction, and abdominal trauma, the most common conditions. I tried to include as many case reports as possible so the reader could have their own opinion about the topic and develop ideas for further research. After completing the manuscript, I read it thoroughly and realized that many things could be written better. Margaret Atwood's tip for writers motivated me to go further: "*If I waited for perfection, I would never write a word.*" Therefore, I would never write this book if I had waited for perfection.

Additionally, it should be mentioned that possibly any cause of acute abdomen can occur during pregnancy, and a detailed description would lead to an enormous number of unnecessary pages. Therefore, a short description of the disease is presented in conditions with only one or several cases published. It is difficult to say if this book is more suitable for gynecologists or general/abdominal surgeons. Some parts will be more interesting to the surgeon, while others to the gynecologist, especially therapeutic considerations. The diagnostic workup will be interesting to every reader. Some photos (figures) in the text are not of excellent quality. Still, because of the extreme rarity of some conditions, it is impossible to obtain other photographs of similar or identical pathology.

And my final plea... to every reader... please contact me about any type of errors, misinterpretations, and medical/surgical mistakes in the text because it would improve (further editions of) this interesting subject. Contact me if you have any questions about the subject. Also, any reader dealing with this subject could feel free to contact me to be an author of one of the chapters in (possible) further editions of this book. My other plea to the reader is to publish cases of the acute abdomen during pregnancy so the medical community could have a better insight into the incidence, etiology, diagnosis, treatment, and maternal and fetal outcome for all causes of the acute abdomen during pregnancy.

I hope the reader will enjoy reading the book as much as I enjoyed creating it!

Zagreb, Croatia

Goran Augustin

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## Part I

### General Considerations

**Abstract**

Imaging studies are necessary for accurate preoperative diagnosis of acute abdominal conditions during pregnancy. However, confusion about the safety of these modalities for pregnant and lactating women and their infants often results in unnecessary avoidance of useful diagnostic tests or interruption of breastfeeding. Ultrasonography and magnetic resonance imaging are not associated with risks. They are the imaging techniques of choice for pregnant patients. However, they should be used prudently and only when their use will answer a relevant clinical question or otherwise provide medical benefit to the patient. With few exceptions, radiation exposure through radiography, computed tomography, or nuclear medicine imaging techniques is at a dose much lower than the exposure associated with fetal harm. If these techniques are necessary after inconclusive ultrasonography or magnetic resonance imaging or are more readily available, they should not be withheld from a pregnant patient. Terminating pregnancy at fetal doses of less than 100 mGy is not justified based on radiation risk. Breastfeeding should not be interrupted after gadolinium administration.

**1.1 General Considerations**

Clinicians may not be well informed of the facts of diagnostic radiological studies in pregnancy. Lack of understanding of radiation effects on the fetus causes unnecessary anxiety in pregnant patients exposed to diagnostic radiation and may lead to unnecessary pregnancy termination. Physicians may be reluctant to order a radiological examination due to the potential teratogenic risks to the fetus and the medicolegal implications of the radiation dose, causing birth defects. For acute indications, the benefits for the mother usually outweigh the small risk to the fetus. The indications for diagnostic imaging modalities are presented in the corresponding chapters.

The greatest radiation effects occur during rapid cell proliferation (2–25 weeks of pregnancy). The recommended total dose of radiation is less than 5 rad. During the first 2–3 weeks of pregnancy, while cells are not yet specialized and radiation injury will cause implantation failure or undetectable death of the embryo. After that, the injury usually occurs in the organs under development during exposure.

Patients and physicians are commonly concerned about fetal radiation exposure, but adverse effects are unlikely at less than 5–10 radiation-absorbed doses (rads) [1, 2]. Less than 1% of trauma patients are exposed to more than 3 rads

(Table 1.1) [1, 3, 4]. However, the risk to the fetus of a 1 rad exposure, approximately 0.003%, is >1000 times smaller than the spontaneous risks of malformations, abortions, or genetic disease. Intrauterine exposure to 10 rad does not cause a significant increase in congenital malformations, intrauterine growth retardation, or miscarriages. However, it is associated with a small increase in childhood cancers. Poor growth, mental retardation, central nervous system defects, and microcephaly are the most common adverse events related to large fetal radiation doses [2]. The relative risk (RR) of childhood cancers is greatest when a fetus is exposed to radiation in the first trimester (RR 3.19) and is high when exposure occurs before 8 weeks of gestation (RR 4.60) [4]. The overall RR of in utero radiation was not statistically different from that of the general population [4]. After 15 weeks of gestation, fetuses are unlikely to be affected by radiation [4]. Fetal doses from identical procedures vary among pregnant women and are lower in obese women [5].

*No single diagnostic procedure results in a radiation dose that threatens the well-being of the developing embryo and fetus. (American College of Radiology [7])*

*The fetal risk is considered to be negligible at 5 rad or less when compared with the other risks of pregnancy, and the risk of malformations is significantly increased above control levels only at doses above 15 rad. (National Council on Radiation Protection [8])*

### 1.1.1 Examinations That Do Not Require Verification of Pregnancy Status

In general, X-ray-based examinations that do not directly expose the pelvis or gravid uterus to the X-ray beam do not require verifying pregnancy status. Such studies include but are not limited to [7]:

- Chest radiography,
- Extremity radiography,
- Any diagnostic examination of the head or neck,
- Mammography,
- Any CT imaging outside of the abdomen or pelvis (except for the hip),
- Nuclear medicine examinations.

### 1.1.2 Examinations That May Require Verification of Pregnancy Status

Examinations in this group include [7]:

- Interventional fluoroscopic procedures of the abdomen or pelvis,
- Diagnostic angiography of the abdomen or pelvis,
- Hysterosalpingography [13],
- Standard-dose CT protocols of the abdomen or pelvis,
- Diagnostic Nuclear Medicine PET/CT.

A refused pregnancy test by the patient should be documented in the patient's medical record, and the radiologist should be notified. When pregnancy is discovered after undergoing an imaging procedure using ionizing radiation, counseling should provide her with information to objectively assess the possible risk to the conceptus [7].

**Table 1.1** Radiation exposure for the unshielded uterus/fetus in various imaging studies

|                                                          | Examination type                          | Estimated fetal dose per examination (mGy = mSv) |                                                       |
|----------------------------------------------------------|-------------------------------------------|--------------------------------------------------|-------------------------------------------------------|
| <b>Estimated fetal exposure for plain X-rays</b>         | Skull                                     | <0.0005                                          |                                                       |
|                                                          | Dental                                    | 0.001                                            |                                                       |
|                                                          | Cervical spine                            | 0.02                                             |                                                       |
|                                                          | Upper or lower extremity                  | 0.01                                             |                                                       |
|                                                          | Chest                                     | 2–7/104                                          |                                                       |
|                                                          | Abdominal                                 | 1.4–4.2                                          |                                                       |
|                                                          | Thoracic spine                            | 0.09                                             |                                                       |
|                                                          | Lumbosacral spine                         | 1.7–10                                           |                                                       |
|                                                          | Pelvis                                    | 1.1–4                                            |                                                       |
|                                                          | Mammogram                                 | 0.2–0.7                                          |                                                       |
|                                                          | Intravenous pyelogram                     | 10–40                                            |                                                       |
|                                                          | Retrograde pyelography                    | 6                                                |                                                       |
| <b>Estimated fetal exposure for fluoroscopic studies</b> | Upper GI series                           | 0.56–1                                           |                                                       |
|                                                          | Barium swallow                            | 1.1–5.8                                          |                                                       |
|                                                          | Barium enema                              | 6.8–10                                           |                                                       |
|                                                          | Cerebral angiography                      | <0.1                                             |                                                       |
|                                                          | Cardiac angiography                       | 0.85                                             |                                                       |
|                                                          | GI = gastrointestinal                     |                                                  |                                                       |
| <b>Estimated fetal exposure for computed tomography</b>  | Head                                      | <0.005                                           |                                                       |
|                                                          | Chest                                     | 0.06–0.16                                        |                                                       |
|                                                          | Chest angiography                         | 0.0035–0.131                                     |                                                       |
|                                                          | Abdomen                                   | 8–30                                             |                                                       |
|                                                          | Lumbar spine                              | 0.9–7.5                                          |                                                       |
|                                                          | Pelvis                                    | 25–79                                            |                                                       |
|                                                          | Pelvimetry                                | 0.2–0.4                                          |                                                       |
| Study                                                    | Estimated activity administered per study | Dose to uterus/embryo (mGy = mSv)                | Estimated fetal exposure for nuclear medicine studies |
| Brain                                                    | 20 mCi <sup>99m</sup> Tc DTPA             | 7–8.8                                            |                                                       |
| Hepatobiliary                                            | 5 mCi <sup>99m</sup> Tc sulfur colloid    | 0.45                                             |                                                       |
|                                                          | 5 mCi <sup>99m</sup> Tc HIDA              | 1.5                                              |                                                       |
| Renal                                                    | 20 mCi <sup>99m</sup> Tc DTPA             | 8.8                                              |                                                       |
| V-Plung scanning                                         |                                           | 0.1–0.37                                         |                                                       |
| Perfusion portion                                        | 3 mCi <sup>99m</sup> Tc MAA               |                                                  |                                                       |
| Ventilation portion                                      | 10 mCi <sup>133</sup> Xe gas              |                                                  |                                                       |
| Thyroid scanning                                         | 0.1 mCi <sup>131</sup> I                  |                                                  |                                                       |
| Whole body (2–6 weeks)                                   |                                           | 0.15                                             |                                                       |
| Whole body (12–13 weeks)                                 |                                           | 1.6                                              |                                                       |
| Whole body (20 weeks)                                    |                                           | 3                                                |                                                       |
| Fetal thyroid (12–13 weeks)                              |                                           | 1300                                             |                                                       |
| Fetal thyroid (20 weeks)                                 |                                           | 5900                                             |                                                       |

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*DTPA* diethylenetriaminepentaacetic acid, *HIDA* hepatobiliary iminodiacetic acid, <sup>131</sup>I iodine-131, *mCi* millicuries, <sup>99m</sup>Tc *MAA* technetium macro-aggregated albumin plus, *V-P* ventilation-perfusion

Average environmental background radiation (cumulative dose over 9 months): 0.5–1.633,34

The accepted background cumulative dose of ionizing radiation during pregnancy is 5 rad (50 mGy), which is much more than the exposure dose of most of the radiological diagnostic examinations

## 1.2 Abdominal Ultrasound

The two major bioeffects from ultrasound (US) are thermal and nonthermal. Nonthermal effects (measured by mechanical index) are secondary to the wave's alternating positive and negative pressures (direct effect). This affects tissues containing gas pockets, such as the lung and intestine. In other tissues, there is no evidence that the diagnostic US produces nonthermal damage without gas-filled contrast agents [9]. Single beam modes (A-mode, M-mode, and spectral pulsed Doppler) have a greater potential for nonthermal hazards than scanned modes (B-mode, Color Doppler), although the use of a narrow write-zoom box increases this potential for scanning modes [9].

The energy absorption in tissue primarily leads to a rise in temperature (thermal effects measured with thermal index—TI). The temperature elevation depends on the spatial-peak temporal average intensity (ISPTA), the US frequency, the dwell time along the beam axis, the width of the beam, the tissue properties, and patient characteristics. The US Food and Drug Administration (FDA) has proposed an upper limit of 720 mW/cm<sup>2</sup> for the spatial-peak temporal average intensity of the US beam for an obstetric US [10]. The British Medical Ultrasound Society made similar recommendations based on thermal indices (Fig. 1.1).

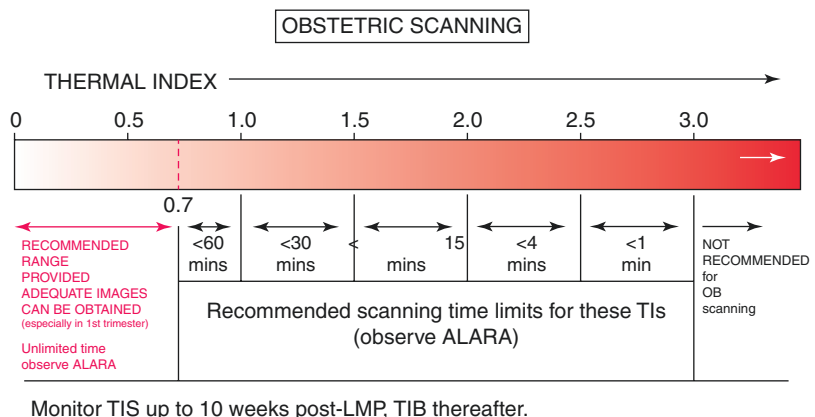
*According to the available evidence, exposure to the diagnostic US during pregnancy appears to be safe. (International Society of Ultrasound in Obstetrics and Gynecology 2009 [11])*

The British Medical Ultrasound Society neonatal cranial examinations via the fontanelle safety guidelines incorporate a limit for the TI in conjunction with the duration of the neonatal cranial scan. They suggest that scanning time should be restricted for any value TI > 0.7. For a TI = 2.3, the duration of such scans should be limited to 4 min, and the neonatal brain scan is not recommended for a TI > 3 (Fig. 1.2). During neonatal cranial scans, the transducer remains stationary over the fontanelle with minimal movement. Therefore, significantly elevated temperatures are more likely [12].

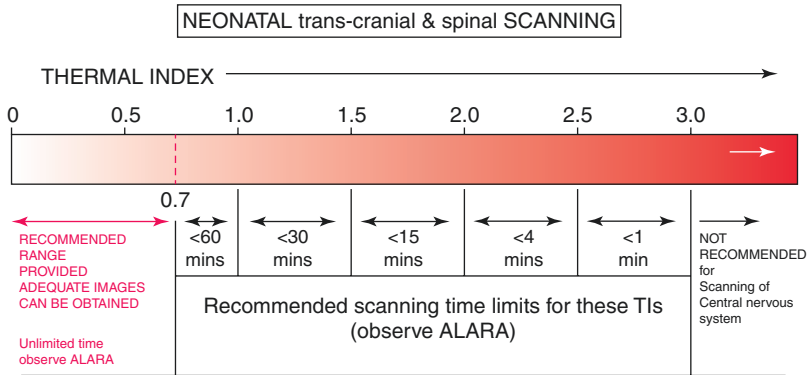
A temperature elevation of 4 °C, maintained for ≥5 min, is potentially hazardous to a fetus or embryo. Some diagnostic US equipment, operating in spectral pulsed Doppler mode, can produce temperature rises over 4 °C in bone, with an associated risk of high temperatures developed in adjacent soft tissues by conduction [9]. From the transvaginal US, the temperature rise in fetal tissue is 0.5–1 °C at 1 cm depth (Fig. 1.3). The contribution to tissue heating at 2 cm and deeper is negligible [14]. Neonatal cranial scans are carried out within 10–15 MHz compared with the 2.5–5 MHz used for obstetric/fetal applications.

Up to 8 weeks after conception, organogenesis occurs. This is when cell damage might lead to fetal anomalies or subtle developmental changes. The brain and spinal cord continue to develop through to the neonatal period. The presence of bone within the beam greatly increases the likely temperature rise due to direct absorption in the bone itself and heat conduction

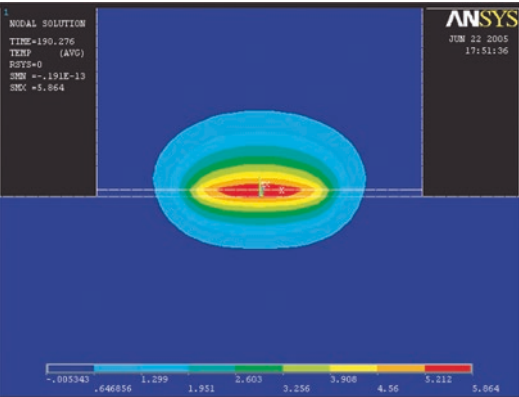
**Fig. 1.1** Recommended maximum scanning times for obstetric examinations conducted with different displayed Thermal Indices (TI) [13]



**Fig. 1.2** Thermal hazard risk should be reduced when exposing the head, brain, or spine of any fetus or neonate to diagnostic ultrasound [13]



Monitor TIC. MI>0.7 should be used with caution in the presence of contrast agents



**Fig. 1.3** Temperature rise variation prediction in a finite-element model after 200 s. The upper segment represents the transducer, and the lower segment represents the tissue mimic. Heat is applied to a thin layer in between, representing the transducer lens. The aspect ratio of the transducer aperture is 3:1, smaller in the direction perpendicular to the image plane. The temperature scale is in °C. (Reproduced with permission from [14])

**Table 1.2** Recommended safety limits for obstetric scans more than 10 weeks gestational age

| TIB     | Recommended scanning time                                  |
|---------|------------------------------------------------------------|
| 0.7–1.0 | Restrict time to <b>60</b> min                             |
| 1.1–1.5 | Restrict time to <b>30</b> min                             |
| 1.6–2.0 | Restrict time to <b>15</b> min                             |
| 2.1–2.5 | Restrict time to <b>4</b> min                              |
| 2.6–3.0 | Restrict time to <b>1</b> min                              |
| >3.0    | Scanning of the fetus is not recommended; however, briefly |

Reproduced with permission from [17]  
TIB thermal index for bone

from bone to adjacent tissues. The following table identifies the relevant landmarks in early pregnancy. The eye is particularly vulnerable to

thermal hazards since the lens and the aqueous and vitreous liquids have no cooling blood supply. This applies to the eye of a person of any age (e.g., a child or adult) and a fetus, although a fetal eye is better cooled due to a liquid environment [13].

Doppler US can produce high intensities and should be used judiciously, keeping the exposure time and acoustic output to the lowest level possible [15]. European Federation of Societies for Ultrasound in Medicine and Biology (EFSUM) statements from 2019 for Doppler use in pregnancy up to 14 weeks are [16]:

- Pulsed Doppler (spectral, power, and color flow imaging) US should not be used routinely,
- When performing Doppler US, the displayed TI  $\leq 1.0$ , and exposure time should be kept as short as possible (usually less than 5–10 min) and should not exceed 60 min,
- There are unlikely fetal safety implications when scanning maternal uterine arteries in the first trimester if the embryo/fetus lies outside the Doppler US beam.

Table 1.2 shows the advised TI for bone levels and recommended safety limits for obstetric scans more than 10 weeks gestational age according to the British Medical Ultrasound Society from 2020.



### 1.3 Abdominal CT

Exposure to less than 5 rad (50 mGy), which includes most imaging radiation doses, is not associated with an increase in fetal anomalies or pregnancy loss (Table 1.3) [7, 18]. Also, fetal risks during normal pregnancy include a 3% risk of spontaneous birth defects, a 15% risk of spontaneous abortion, a 4% risk of prematurity and growth retardation, and a 1% risk of mental retardation [19]. This should be explained to the future mother.

CT is used when the US examination is not diagnostic and unequivocal. The risk and benefits should be weighed for every pregnant patient.

It is preferable to use the multidetector-row CT with the high-speed mode in pregnancy since it has half the radiation dose of the high-quality mode, and its scanning parameters are identical. Radiation exposure in these settings is 300 mrad, below an accepted safe level of radiation exposure in pregnancy of 5 rad. The radiation may increase the background incidence of cancers before the age of 20 by 0.06%/rad delivered to the fetus [4, 20]. These are the results of

15–20 years ago. The consequences of newer CT modules with lesser radiation will be evident in the following decades. Table 1.3 shows potential dose-dependent radiation effects during fetal development.

Lack of understanding of radiation effects on the fetus causes unnecessary anxiety in pregnant patients and clinicians exposed to diagnostic radiation and may lead to unnecessary pregnancy termination. Family physician perceptions from 2004 of teratogenic risk associated with undergoing plain radiography and CT during early pregnancy showed that 3% would recommend pregnancy termination after the first trimester CT and 0.5% following radiography in the first trimester; 12% were unsure if pregnancy termination was needed after radiography; and 19% were unsure about a need for CT examination. Also, 8% of obstetricians would recommend pregnancy termination after the first trimester CT examination [21]. A further decrease in radiation is a low-dose CT. In 2004, the largest single radiation dose was 1.372 rad, significantly lower than an average of 2.2 rad for detecting urinary stones [22].

**Table 1.3** Potential in utero-induced radiation effects

| Conception age    | <50 mGy     | 50–100 mGy                                                                 | >100 mGy                                                                                               |
|-------------------|-------------|----------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| Before conception | <i>None</i> | None                                                                       | None                                                                                                   |
| 1st–2nd week      | <i>None</i> | Probably none                                                              | Possible spontaneous abortion                                                                          |
| 3rd–8th week      | <i>None</i> | Potential effects are uncertain and too subtle to be clinically detectable | Possible malformations increase as the dose increases                                                  |
| 9th–15th week     | <i>None</i> | Potential effects are uncertain and too subtle to be clinically detectable | Risk of diminished IQ or mental retardation, increasing in frequency and severity with increasing dose |
| 16th–25th week    | <i>None</i> | None                                                                       | IQ deficits are not detectable at diagnostic doses                                                     |
| >25th week        | <i>None</i> | None                                                                       | None applicable to diagnostic medicine                                                                 |

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## 1.4 Abdominal MRI

MRI offers superior contrast resolution relative to any other available imaging modality. It detects small amounts of fluid and mild inflammation even without IV contrast, by employing T2-weighted sequences. MRI is the diagnostic method of choice when the radiation risk or potential nephrotoxicity of iodine-based contrast agents is a major concern. Noncontrast MRI is beneficial as a radiation-free modality for populations more vulnerable to ionizing radiation—specifically pediatric and pregnant patients. No evidence exists on specific consequences of non-contrast MRI on children or fetuses exposed during any trimester [23, 24] and pregnant adult patients [24].

The disadvantages of MRI are primarily the increased cost and relatively limited availability of MRI equipment or trained personnel compared to US or CT, especially in emergency settings. MRI is not free of theoretical risks, including (1) the potential biological effects of the static and time-varying magnetic fields, (2) the heating effects of the radiofrequency pulses ( $>1.5$  T), and (3) the acoustic noise generated by the spatial encoding gradients [25]. However, no reports of adverse effects from MRI during pregnancy on the developing conceptus exist [26].

Radiofrequency energy in MRI deposits as heat in the tissues. Therefore, all MRI machines monitor the specific absorption rate to comply with safety guidelines. With a limited ability to regulate temperature independently, the developing embryo and fetus depend entirely on the mother's thermoregulatory capacity. As a general rule, maternal core body temperature increases of  $\sim 2$  °C above normal for extended periods,  $2\text{--}2.5$  °C above normal for 0.5–1 h, or  $\geq 4$  °C above normal for 15 min have resulted in developmental abnormalities in animal models [27]. Corresponding specific absorption rate (SAR) values that would be necessary to cause such temperature elevations in a healthy adult female would be in the range of  $\geq 15$  W/kg (whole-body average or WBA), with  $\sim 4$  W/kg required to increase core temperature 1 °C. A conservative estimate of 1.5 W/kg WBA (1/10th the threshold

to protect against measurable temperature increases) would seem sufficient to protect against any significant blood flow reduction to the pregnant mother's embryo or fetus [27]. This is more than three times above the current WBA limit for occupational exposure (0.4 W/kg) as outlined in IEEE C95.1-2005 and ICNIRP-1998 international safety standards for radiofrequency exposures. The maximum localized specific absorption rate occurs in the mother, with approximately 50% in the fetus, and no studies have demonstrated the effects on the fetus [28, 29]. Specific recommendations for MRI use in pregnancy are:

- When scanning a pregnant woman, if the fetus or maternal abdomen is not the target organ, the fetus should be kept out of the transmit field of the RF coil if possible,
- Care must be taken when scanning fetuses with poor placental function, such as fetal growth restriction. It should be noted that maternal heat stress has been reported to reduce placental perfusion,
- Care must be taken when scanning pregnant women with conditions leading to impaired thermoregulation. Unless the clinical situation dictates that the scan is urgent, it would be prudent not to scan pregnant women who are febrile.

Exposure to 1.5 T noncontrast MRI during pregnancy had no harmful effects on long-term neurodevelopmental outcomes [30].

The patient should be informed that there are no known harmful effects from the use of MR imaging at 1.5 T or lower magnetic field strengths [25] and that there is a lack of experience with the use of field strengths greater than 2.5 T, and these should be avoided [25]. Despite obvious improvements in the image quality at 3 T, the specific absorption rate usually increases significantly [31]. Two-channel radiofrequency (RF) shimming can improve imaging without increasing the specific absorption rate for fetal MRI at 3 T [31].

Absolute contraindications for MR include [32]:

- metal implants not made of titanium,
- metal implants of unknown composition,
- gadolinium administration during the first trimester.

The intermediate and lowest-risk gadolinium-based contrast media may be given to pregnant women in the lowest dose required to provide essential diagnostic information [33]. Gadolinium-based MR contrast agents pass through the placenta to fetal circulation. The fetal kidneys then excrete the contrast material into the amniotic fluid, where the agent can remain for an indeterminate amount of time. No large, well-controlled studies have been performed to document the presence or absence of adverse fetal effects resulting from maternal gadolinium administration. Therefore, the potential risks to the fetus remain unknown [32]. Rapid-sequence MRI is preferable to conventional MRI due to its shorter exposure [34].

*Informed consent should be signed by the patient. The safety of MRI for the fetus has not been proved (US FDA guidelines and the American College of Radiology).*

1.5 MRCP

The European Society of Urogenital Radiology (ESUR) established its Contrast Media Safety Committee in 1994. Table 1.4 presents the ESUR guidelines (version 10.0) from 2018 on using iodine-based and gadolinium-based contrast media during pregnancy [35].

IV iodinated contrast crosses the placenta and is classified as an FDA category B drug. A known risk is free iodine uptake by the fetal thyroid gland early in pregnancy, potentially inducing a hypothyroid state. Animal studies with IV iodinated contrast have shown no fetal risk, but without controlled studies on pregnant women, theoretical risks remain [36]. American College

**Table 1.4** ESUR guidelines for using iodinated and gadolinium contrast media during pregnancy and lactation

|                                                    | Iodine-based contrast media                                                                                                                                                                                                                                                                                     | Gadolinium-based contrast media                                                                                                                                                                                                                                                                  |
|----------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Pregnancy                                          | In exceptional circumstances, when radiographic Examination is essential, iodine-based contrast media may be given to the pregnant female<br>b) Following administration of iodine-based contrast media to the mother during pregnancy, thyroid function should be checked in the neonate during the first week | (a) When there is a very strong indication for enhanced MR, the smallest possible dose of a macrocyclic gadolinium contrast agent may be given to the pregnant female<br>(b) Following administration of gadolinium-based agents to the mother during pregnancy, no neonatal tests are necessary |
| Lactation                                          | Breastfeeding may be continued normally when iodine-based contrast media is given to the mother                                                                                                                                                                                                                 | Breastfeeding may be continued normally when macrocyclic gadolinium-based contrast agents are given to the mother                                                                                                                                                                                |
| Pregnant or Lactating mother with renal Impairment | Follow ESUR guidelines for contrast media administration when renal function is impaired. No additional precautions are necessary for the fetus or neonate                                                                                                                                                      | Do not administer gadolinium-based contrast agents                                                                                                                                                                                                                                               |

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of Radiology Committee on Drugs and Contrast Media claims that iodinated contrast medium does not affect thyroid function test results in patients with a normally functioning thyroid gland. Multiple studies have shown that a single dose of iodinated contrast medium administered to a pregnant mother does not affect neonatal thyroid function [37].

An additional concern about the safety of MRCP in the first trimester exists because radio-frequency pulses result in energy deposition and potentially result in tissue heating (see Sect. 1.4).

## 1.6 Nuclear Medicine Examinations

Many nuclear medicine examinations do not require routine pregnancy testing (Table 1.5), and most examinations are not indicated in an emergency.

**Table 1.5** Diagnostic nuclear medicine examinations that do NOT require routine pregnancy testing

| Radiopharmaceutical           | Type of scan                                                                                                             |
|-------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| <i>Single photon emitters</i> |                                                                                                                          |
| 99mTc-DTPA                    | Renal scan, ventilation, gastric emptying, VP/VA shunt                                                                   |
| 99mTc-MDP                     | Bone scan                                                                                                                |
| 99mTc-sulfur colloid          | Gastric emptying, bone marrow mapping, Splenule / splenosis localization, sentinel node localization, lymphoscintigraphy |
| 99mTc-Pertechnetate           | Thyroid scan, Meckel's diverticulum                                                                                      |
| 99mTc-MAA                     | Lung perfusion, right-to-left shunt assessment, liver shunt assessment                                                   |
| 99mTc-labelled RBC            | GI bleeding, MUGA, hemangioma                                                                                            |
| 99mTc-HIDA                    | Cholecystitis, bile leak, functional gallbladder disorder                                                                |
| 99mTc-Sestamibi               | Cardiac stress test, parathyroid localization, molecular breast imaging                                                  |
| 99mTc- HMPAO                  | Brain death scan                                                                                                         |
| 111In-WBC                     | Infection, inflammatory bowel disease                                                                                    |
| 111In-Octreoscan              | Neuroendocrine tumor imaging                                                                                             |
| 111In-DTPA                    | Cisternography, CSF leak                                                                                                 |
| 133Xe                         | Lung ventilation                                                                                                         |
| 67Ga                          | Spine infection                                                                                                          |
| 201Tl <sup>a</sup>            | Cardiac perfusion scan stress/rest                                                                                       |
| 133Xe                         | Ventilation                                                                                                              |
| <i>Positron emitters</i>      |                                                                                                                          |
| 18F-FDG                       | Tumor imaging                                                                                                            |
| 68Ga-DOTATATE                 | Neuroendocrine tumor imaging                                                                                             |

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<sup>a</sup>Not commonly used

## 1.7 Radiologic Interventional Techniques

Radiologic interventional techniques are increasingly used. The advantage is minimal invasiveness, while the disadvantage is ionizing radiation. All principles for CT (see Sect. 1.3) or MRI (see Sect. 1.4) use should be applied.

## 1.8 ERCP

### 1.8.1 Radiation

The first report of ERCP during pregnancy in 1990 included five successful cases of biliary sphincterotomy and gallstone extraction for choledocholithiasis or cholangitis [38]. Hoffman and Cunningham, in 1992, reported four pregnant women who underwent ERCP during the first trimester. Radiation exposure after appropriate abdominal shielding is well below levels at which damage to the fetus can occur [39]. The radiation used during ERCP is 18–310 mrad [40, 41]. The *American College of Obstetricians and Gynecologists* (ACOG) states that risks for fetal anomalies, growth restriction, or abortions are not increased with radiation exposure of less than 5 rad, a level above the exposure range for diagnostic procedures [42]. Radiation risk is greatest during the first trimester. Fluoroscopy generally delivers a radiation dose of up to 20 rads/min, but varies depending on the X-ray equipment, patient positioning, and patient size. The fetus should be shielded during cholangiography. Other alternatives to fluoroscopy include intraoperative US and choledochoscopy. Recently, more ERCP procedures have been performed without fluoroscopy to eliminate the radiation risk [43, 44], mainly as a two-stage approach. Biliary drainage is done in the first ERCP, primarily used during

the third trimester when the completion of pregnancy is near. Biliary sphincterotomy with the small incision as a first-stage ERCP avoids biliary AP caused or aggravated by stent-induced pancreatic duct obstruction and dislodgement or early fall-off of the plastic stent due to the large incision. Then after delivery, the second ERCP with the definitive extraction of calculi under fluoroscopic control is performed [43]. Even though the risks to the fetus during the second and the third trimester for radiation exposure are low, it is recommended to protect the uterus with a lead shield.

ERCP done by experienced endoscopists is a safe procedure during pregnancy. Radiation-free techniques appear to reduce the rates of nonpregnancy-related complications but not fetal and pregnancy-related complications [45].

### 1.8.2 Techniques

Solely diagnostic ERCP is not recommended during pregnancy [46].

In the general population, diagnostic ERCP is not recommended and has been replaced by less invasive tests such as endoscopic ultrasound (EUS) and magnetic resonance cholangiopancreatography (MRCP) [47].

Eliminating radiation exposure can be accomplished by cannulating the CBD with a sphincterotome over a guidewire that can be fixed in place, sphincterotomy, exchanging the sphincterotome for an extraction balloon catheter over the guidewire, and sweeping the bile duct without a cholangiogram to extract any stones. This technique does not provide real-time information regarding the anatomy of the ductal system and documentation of stone clearance [44]. Another

option is capturing fluoroscopic images with a videoendoscopy, providing a safer ERCP procedure than spot radiography [48]. The third option is sphincterotomy under US guidance [49]. US-guided ERCP showed a higher rate of stone clearance in comparison to empirical non-radiation-ERCP (89% vs. 60%,  $P < 0.05$ ) and lower complication rates (14% vs. 3%,  $P < 0.05$ ) [50]. EUS can be carried out in the same session before ERCP to determine the number, size, and site of stones [51]. Another way to confirm biliary cannulation and stone clearance without radiation is by inserting a choledochoscope through the working channel of EGD to visualize the bile duct [52] directly.

The bile aspiration after deep cannulation enables confirmation of selective CBD cannulation and endoscopic sphincterotomy without radiographic control, including US [53]. One modification includes CBD cannulation with a double-lumen sphincterotome. With deep cannulation, the bile confirms the CBD position. After deep CBD cannulation, the guidewire is passed, and a complete biliary sphincterotomy is done over the guidewire. When deep CBD cannulation is not possible, after two attempts, the conventional sphincterotome is removed and needle-knife sphincterotomy is performed. Once the biliary orifice is identified, a complete biliary sphincterotomy is performed using a conventional double-lumen sphincterotome after confirming the location inside CBD. After the biliary sphincterotomy, a Zag guidewire is left in place, and a 7Fr double pigtail stent is placed in the CBD. Patients are kept nil orally for 6 h after the procedure, and IV fluids and IV cefotaxime 1 g bid are given for 1 day, followed by oral antibiotics for 5–7 days. After delivery, all the patients are subjected to definitive ERCP. Biliary stents are removed, and a cholangiogram is obtained. All small stones are removed with a Dormia basket. For retaining large stones, mechanical lithotripsy is used. Patients with multiple large stones undergo surgery [54]. The aspiration technique avoids pancreatography. Fluoroscopy time should be as short as possible (<1 min), and spot radiographs should be avoided if possible [55].

### 1.8.3 Contrast Agents

Among other considerations for ERCP in pregnancy, contrast agents containing iodine, such as diatrizoate, can cause hypothyroidism in the baby. Risks may be minimized by using low concentrations of diatrizoate, especially the water-soluble form, thus limiting the number of intraductal injections and avoiding unnecessary pancreatography [56]. Guidelines for contrast media use during pregnancy are listed in Table 2.2.

### 1.8.4 Maternal and Fetal Outcomes

Nonradiation techniques may decrease the risk of nonpregnancy-related outcomes but do not impact fetal or pregnancy-related outcomes [45]. The long-term outcome in children born after radiation exposure during ERCP was unremarkable [57].

## 1.9 Endovascular Techniques

Endovascular techniques have been increasingly used in the pregnant population. Most procedures include interventions in the upper maternal abdomen because the fetus can be protected from radiation exposure by a lead apron [58, 59].

### 1.10 Intraoperative Cholangiography

Fetal radiation exposure in routine IOC is equivalent to 0.5 rad, well below the threshold dose of 5–10 rad recommended in pregnancy. Therefore, it is considered safe, primarily when used with uterine shielding [60]. A shield to cover the fetus is recommended in all trimesters [61, 62].

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# Anesthetic and Perioperative Management

## 2

### Abstract

To provide safe anesthesia for mother and fetus following goals should be reached: (1) optimization and maintenance of normal maternal physiological function, (2) optimization and maintenance of uteroplacental blood flow and oxygen delivery, (3) avoidance of unwanted drug effects on the fetus, (4) avoidance of stimulating the myometrium (oxytocic effects), (5) avoidance of maternal awareness during general anesthesia, and (6) use of regional anesthesia, if possible. Sugammadex rapidly reverses neuromuscular blockade without fetal harm. Antibiotics and thromboprophylaxis are the most common medications administered for acute abdomen during pregnancy. Antibiotics should be administered according to the FDA drug classes. Anesthetic management is challenging in patients with abdominal trauma or polytrauma when in addition to hemorrhagic shock, there are problems with the patient's airway management. Preoperative and postoperative fetal monitoring is essential for early recognition of fetal distress, influencing the timing and type of combined obstetric and surgical intervention.

### 2.1 Anesthetic Management

Before discussing anesthesiologic issues related to the acute abdomen during pregnancy, it is important to stress that a delay in indicating and performing necessary surgery leads to worse maternal and fetal outcomes.

*A pregnant woman should never be denied medically necessary surgery or have that surgery delayed regardless of trimester because this can adversely affect the pregnant woman and her fetus. (ACOG 2019 [1])*

To provide safe anesthesia for the mother and fetus, following goals should be reached:

- optimization and maintenance of normal maternal physiological function,
- optimization and maintenance of uteroplacental blood flow and oxygen delivery,
- avoidance of unwanted drug effects on the fetus,
- avoidance of stimulating the myometrium (oxytocic effects),
- avoidance of maternal awareness during general anesthesia,
- use of regional anesthesia, if possible.

## 2.1.1 Anesthetic Medications

### 2.1.1.1 General Anesthesia

Anesthetic concerns in the pregnant patient include two major categories: teratogenicity of the anesthetic agents and maternal physiological changes resulting from anesthetic agents. Therefore, strategies to minimize maternal and fetal exposure to anesthetics are essential (Table 2.1).

The teratogenicity of anesthetic agents, resulting in fetal chromosomal damage or carcinogenesis, is minimal. Any morbidity to the fetus is considered primarily from the underlying disease, not the anesthetic agent [2, 3]. There is no increased rate of congenital anomalies with different types of anesthesia used in surgery during pregnancy [4, 5]. In a consensus statement published in the *New England Journal of Medicine* in 2000, no anesthetic agents were listed as definitively causative of fetal malformations [6]. Although without clinical teratogenic outcomes, the theoretical risk should not

be completely disregarded. Many agree that surgery during the first trimester, the period of organogenesis, should be avoided if not emergent [3, 7, 8]. Table 2.2 shows the list of common anesthetic drugs and their classification per FDA category.

Several points should be stressed when considering the possible teratogenicity of various anesthetic agents. First, the background incidence of congenital anomalies in humans is approximately 3%. Second, physiologic derangements such as hypoxemia, hypercarbia, stress, and hypotension may be teratogenic. These problems can occur during anesthesia and surgery and sometimes exist preoperatively [10].

*No currently used anesthetic agents have been shown to have any teratogenic effects in humans when using standard concentrations at any gestational age. (ACOG 2019 [1])*

**Table 2.1** Strategies to minimize patient exposure to and dose and duration of anesthetics

| Type of surgery              | Anesthetic technique                                                                          | Suggested modification/recommendation                                                                                           |
|------------------------------|-----------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|
| Obstetric                    | Neuraxial (epidural or spinal) utilizing local anesthetics ± opioids                          | None                                                                                                                            |
| Non-obstetric (non-emergent) | Neuraxial as above (if applicable) or                                                         | None                                                                                                                            |
|                              | General anesthesia utilizing inhalational agents                                              | <3 h duration—No change<br>>3 h durations—consider deferring until postpartum                                                   |
| Non-obstetric (emergent)     | General anesthesia utilizing inhalational agents                                              | Limit times:                                                                                                                    |
|                              |                                                                                               | (a) Between induction and start of surgery and<br>(b) Between end of surgery and end of anesthesia                              |
| Fetal procedures             | Local anesthesia                                                                              | No change                                                                                                                       |
|                              | Neuraxial anesthesia                                                                          | No change                                                                                                                       |
|                              | IV sedative—hypnotic—propofol                                                                 | <3 h duration—no change                                                                                                         |
|                              |                                                                                               | >3 h duration—discuss risk/benefit                                                                                              |
|                              | IV sedative—Midazolam                                                                         | Consider IV opioids (fentanyl or remifentanyl) or IV dexmedetomidine                                                            |
|                              | General anesthesia with inhalational agents                                                   | <3 h duration—no change<br>>3 h duration—discuss risk/benefit                                                                   |
|                              | General anesthesia with increased concentration of inhalational agents for uterine relaxation | Consider supplementing with magnesium sulfate, Atosiban <sup>a</sup> or Nitroglycerin <sup>b</sup> for intraoperative tocolysis |

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IV intravenous

<sup>a</sup>Atosiban is not approved for use in the USA by the FDA

<sup>b</sup>Nitroglycerin is difficult to titrate to effect, may result in intractable hypotension and/or pulmonary edema

**Table 2.2** The placental transfer characteristics of commonly used anesthetic drugs

| Drug                     | Properties                                            | Placental transfer | Remarks                                                                                                                                   |
|--------------------------|-------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Induction agents</b>  |                                                       |                    |                                                                                                                                           |
| Thiopental               | Highly lipid soluble, weak acid                       | +++                | Quickly cleared by neonate after delivery                                                                                                 |
| Propofol                 | Lipid soluble                                         | +++                | Transient depression of Apgar score and neurobehavioral effects in neonate                                                                |
| Ketamine                 | Weak base                                             | ++++               | F/M ratio 1.26 occurs within 2 min of intravenous bolus                                                                                   |
| <b>Inhalation agents</b> |                                                       |                    |                                                                                                                                           |
| Volatile anesthetics     | Highly lipid soluble; low molecular weight            | +++                | Greater sedative effect on neonate if dose-delivery interval is prolonged                                                                 |
| Nitrous oxide            |                                                       | ++                 | Possible diffusion hypoxia in neonate                                                                                                     |
| <b>Opioids</b>           |                                                       |                    |                                                                                                                                           |
| Morphine                 | Less lipid soluble; but low protein-binding           | ++                 |                                                                                                                                           |
| Fentanyl                 | Lipid soluble                                         | +++                |                                                                                                                                           |
| Pethidine                | Only 50% plasma protein bound                         | ++                 | Prolonged neonatal depression due to increased half-life of meperidine and its metabolite—normeperidine                                   |
| Remifentanyl             |                                                       | +                  | No adverse fetal effects as rapidly metabolized by fetus                                                                                  |
| Naloxone                 |                                                       | +++                | Though short-term safety of naloxone is well documented, it should be used only in cases of absolute or relative maternal opioid overdose |
| Benzodiazepine           | Highly lipid soluble                                  | ++                 | More neonatal depression, midazolam—less placental transfer than diazepam                                                                 |
| NM blockers              | Large molecules; poorly lipid soluble; highly ionized | –                  | No significant clinical effects on fetus                                                                                                  |
| <b>Anticholinergics</b>  |                                                       |                    |                                                                                                                                           |
| Atropine                 | Lipid soluble; tertiary amine                         | ++                 |                                                                                                                                           |
| Glycopyrrolate           | Fully ionized; quaternary ammonium compound           | –                  |                                                                                                                                           |
| Neostigmine              | Quaternary ammonium compound; but a small molecule    | +++                | May cause fetal bradycardia; hence it is better to add atropine to neostigmine in incidental surgery during pregnancy                     |
| <b>Local anesthetics</b> |                                                       |                    |                                                                                                                                           |
| Lignocaine               | Less lipid soluble; low protein binding               | ++                 | Can accumulate in the fetus due to “ion trapping” if the fetus becomes acidotic                                                           |
| Bupivacaine; ropivacaine | Highly lipid soluble; but high protein binding        | ++                 |                                                                                                                                           |

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*F/M* fetal/maternal, *NM* neuromuscular

The drugs crossing the placenta may be categorized into three types. In type 1 (e.g., thiopental), the complete transfer occurs with equilibrating maternal and fetal blood concentrations. In type 2 (e.g., ketamine), the drug reaches a higher concentration in fetal blood than maternal blood. Only a minimal amount reaches the fetal blood in type 3 (e.g., succinylcholine).

Sugammadex encapsulates rocuronium and vecuronium molecules, aminosteroid agents

commonly used in general anesthesia [11]. The combination of rocuronium and sugammadex for rapid-sequence induction combines rapid onset and rapid reversal of neuromuscular blockades with avoidance of severe side effects. It is a very comfortable combination during Cesarean section (CS) [12]. Although the impact of pregnancy on the volume of distribution of sugammadex is unknown, the effectiveness of rocuronium block reversal following 2 or 4 mg/kg sugammadex has

been confirmed [13]. Rapid neuromuscular blockade reversal is confirmed in myasthenia gravis patients during CS [14].

There is concern about sugammadex's ability to encapsulate progesterone and reduce progesterone levels. Interaction with hormonal contraceptives raises the question of the adverse effects of sugammadex administration on the maintenance of the first trimester of pregnancy. A study on rats in the first trimester of pregnancy did not show adverse effects. They did not affect the successful completion of pregnancy without stillbirth or miscarriage [15]. In a case series of pregnant patients undergoing non-obstetric surgery, all fetuses showed good vitality in the cardiotocogram performed after the procedure. All

babies are healthy, without congenital abnormalities [16]. Sugammadex's effects on female reproductive function, pregnancy, and puerperium are presented in Table 2.3.

Magnesium sulfate is used to prevent uterine contractions and preterm labor (see Sect. 4.6.2.1), enhancing the effect of rocuronium. It does not significantly affect the efficacy of sugammadexin, reversing rocuronium-induced neuromuscular blockade [18].

### 2.1.1.2 Sedation and Spinal Anesthesia

Sedation in pregnancy has always been a challenge to anesthetists. During ERCP in pregnant patients, sedation could have side effects from the maternal prone position. Therefore, fetal and maternal moni-

**Table 2.3** Effects of Sugammadex on female reproductive function, pregnancy, delivery, and lactation [17]

| Context                           | Current evidence                                                                                                                                                                                                                                                                                                                   | Research gaps                                                                                                                                                                |
|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Women of reproductive potential   | In vitro studies (unpublished) indicate that sugammadex binds progesterone, theoretically reducing hormone levels to an extent that is equivalent to missing dose(s) of hormonal contraception (oral, IUD, injectable). This has prompted manufacturer to recommend barrier contraception for 1 week following sugammadex exposure | Actual clinical risk of unintended pregnancy due to contraceptive failure after sexual intercourse without barrier contraception following sugammadex exposure is unknown    |
| Maintenance of early pregnancy    | Single preclinical study: high-dose sugammadex (30 mg/kg) administered to first trimester pregnant rats failed to reduce endogenous progesterone levels or alter live birth or stillbirth rates                                                                                                                                    | No human evidence                                                                                                                                                            |
| Maternal–fetal placental transfer | Large molecular mass and polarization in aqueous solution predict limited placental transfer                                                                                                                                                                                                                                       | No evidence regarding placental transfer                                                                                                                                     |
| Fetal effects                     | Primary cell cultures: Sugammadex alone in clinically relevant concentrations has been reported to promote neuronal apoptosis in primary cultures, possibly due to oxidative stress from depletion of neuronal cholesterol                                                                                                         | Limited preclinical evidence. No human evidence                                                                                                                              |
|                                   | Mice: No neuronal apoptosis (healthy, mature blood–brain barrier is impermeable to sugammadex). Sugammadex combined with sevoflurane, which disrupts blood–barrier integrity, results in greater degree of neuronal apoptosis than sevoflurane alone                                                                               |                                                                                                                                                                              |
| Cesarean delivery                 | Sugammadex reversal of rocuronium is reported to be safe and effective in parturients at the end of CD surgery. This includes patients with profound NMB (1 posttetanic twitch) reversed with 4 mg/kg (actual body weight)                                                                                                         | Effectiveness of sugammadex rescue reversal in cannot intubate/cannot ventilate after 1–1.2 mg/kg rocuronium (rapid sequence induction) has not been established or reported |
| Lactating women                   | Single preclinical study (unpublished) demonstrated peak sugammadex milk levels 30 min after maternal administration in postnatal rats without detectable adverse effects on offspring                                                                                                                                             | No evidence exists regarding the presence of sugammadex in human breast milk                                                                                                 |

toring is mandatory [19, 20]. Following electrocardiography, noninvasive blood pressure measurement, pulse oximetry, and fetal heart rate monitoring (FHR) devices are applied. Insufflation of oxygen at a flow rate of 6 L/min is maintained throughout the procedure. The patients are placed in a left lateral to a prone position. Fetal shielding is accomplished with a lead apron placed between the radiation source and the patient. Although there is no proof of human teratogenicity for anesthetic drugs, inhaled or local, all agents administered during pregnancy must be used with caution and vigilance. Currently, the best options are propofol, midazolam, and fentanyl. Propofol is preferred as a short-acting agent because it can be titrated easily and has a good recovery, with a low incidence of nausea and vomiting. Alternatively, midazolam can be used because of its specific amnesic and anxiolytic properties. The analgesic component of this sedation regimen is opioids. All drugs are given in incremental doses to prevent hemodynamic and respiratory changes in the mother and fetus during the procedure. The most commonly conscious sedation is achieved and maintained with intravenous midazolam 3–5 mg and duodenal hypomotility induced by hyoscine-N-butylbromide 20 mg [21].

*In utero human exposure to anesthetic or sedative drugs has no effect on the developing brain, and no animal data support an effect with exposures less than 3 h. (ACOG Committee opinion 2019 [1])*

Spinal anesthesia is widely used for CS. Although safe, nausea, vomiting, and hypotension are frequent after spinal anesthesia despite prehydration and left uterus displacement [22]. This is attributed to the greater aortocaval compression and greater cephalad spread of sensory blockade by an enlarged uterus. MRI shows a gestation-related reduction in cerebrospinal fluid volume and dural sac surface area associated with the engorged veins in the epidural space [23]. The question is whether spinal anesthesia is effective in conditions with increased intra-abdominal pressure (IAP).

Whether spinal local anesthetic spread in pregnant patients shows the association between pre-incision IAP and maximum sensory block levels is unclear [24, 25].

With an inguinal hernia, severe postoperative complications are lower under local anesthesia, including fewer postoperative analgesic requirements and fewer micturition problems [26]. Operating under general anesthesia in emergency settings is better due to possible unexpected intraoperative findings.

### 2.1.2 Airway Management

Airway management becomes particularly problematic due to the physiologic changes during pregnancy. Increased oxygen consumption and mechanical displacement of the abdominal organs cause the pregnant patient to increase minute ventilation, primarily through a 30–40% increase in tidal volume [27]. A compensatory respiratory alkalosis with a PaCO<sub>2</sub> from 30 to 35 mmHg develops. End-tidal CO<sub>2</sub> monitoring should be used intraoperatively.

The success of regional anesthesia in this population owes its popularity mainly to the airway complications that general anesthesia entails. Airway complications are more prevalent in a parturient receiving general anesthesia than those having regional techniques [28]. Unique issues for the gravid patient in airway management are:

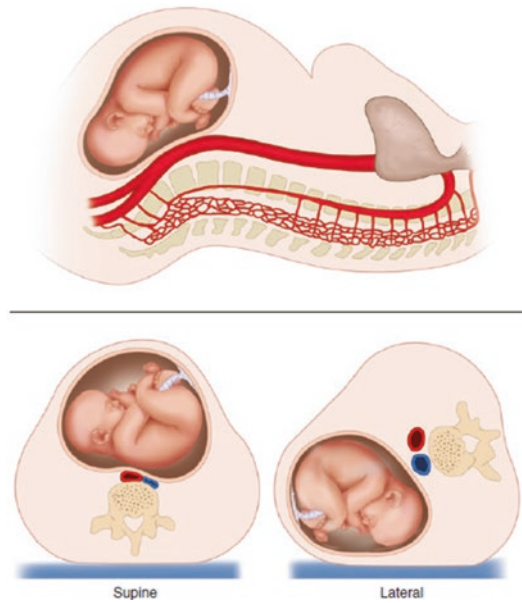
- increased risk of aspiration due to delayed gastric emptying and decreased lower esophageal sphincter tone in combination with increased intra-abdominal pressure,
- despite the safety of rapid-sequence intubation in pregnancy, because of lower serum pseudocholinesterase levels in pregnancy, using a lower dose of succinylcholine during induction is recommended,
- both depolarizing and nondepolarizing muscle relaxants cross the placenta. Effects of these drugs on CTG pattern and fetal activity might lead to a falsely non-reassuring tracing and non-indicated intervention.

A nasogastric tube inserted in a semiconscious or unconscious, injured pregnant woman prevents aspiration of gastric contents [29].

Additionally, vascular engorgement of the respiratory tract during pregnancy may lead to tracheal intubation difficulties. Edema in the airways leads to friable tissues, increased potential for bleeding, and the necessity to use smaller-sized endotracheal tubes in the parturient [30]. Because decreased lower esophageal sphincter pressure and delayed gastric emptying in pregnancy can cause an increased risk of aspiration, cricoid pressure prevents aspiration during intubation [31]. Therefore, rapid-sequence intubation is preferred for the parturient facing an emergent abdominal operation with a full stomach [30]. Also, the underlying cause of acute abdomen, intraoperative strategy, and possible intraoperative complications mandates general anesthesia.

Other compounding airway issues include weight gain, increased breast size, decreased functional residual capacity, increased oxygen consumption, and the potential for aortic and venocaval compression in the supine position during intubation. These issues may lead to rapid desaturation, potentially lower cardiac output, placental-fetal compromise, and asphyxia during delayed attempts at securing the parturient's airway. In addition to these physiologic changes, disease-induced hypotension should be treated initially with aggressive intravenous fluid resuscitation. If possible, the patient should be placed in the left lateral decubitus position to decompress the inferior vena cava to increase venous return (Fig. 2.1). Trendelenburg positioning can also increase the venous return in the hypotensive patient [2].

General endotracheal anesthesia is preferred for CS to manage acute abdomen and early postoperative period. General anesthesia allows greater hemodynamic control and facilitates management of the acid-base status, especially in patients receiving epoprostenol for CVVH in acute pancreatitis during pregnancy. Anticoagulation is better titrated, including heparin in sepsis. Postoperative ventilatory support in ICU permits the resolution of acidosis.



**Fig. 2.1** Left lateral tilt relieves pressure on inferior vena cava in pregnant women

### 2.1.2.1 Diaphragmatic Hernia

The affected side is placed uppermost if a hernia is approached through a thoracotomy [32]. Mediastinal shift, which compromises venous return and collapse of the lower lung, may be worsened by positional compression from the herniated dilated viscera. A rapid-sequence induction is indicated because the patient is at risk of pulmonary aspiration.

General anesthesia and positive-pressure ventilation may be advantageous with atraumatic diaphragmatic hernia to expand the atelectatic lung, increase functional residual capacity, and deliver high oxygen concentrations. Lung ventilation must be undertaken with low tidal volume or low airway pressure until the abdominal contents have been removed from the chest or until a thoracotomy has been performed. Cardiovascular collapse might occur during positive-pressure ventilation. The re-expanded lung previously compressed by herniated viscera may shift mediastinal structures, and venous return may be impeded [33, 34]. Increased pleural pressure from mechanical ventilation is transmitted to the abdomen. It results in an increased upward displacement of the viscera toward the diaphragm and may worsen cardiovascular collapse [34]. A surgeon must be ready to operate before ventilation is begun [33].



Premedication with an H<sub>2</sub> antagonist, metoclopramide, and sodium citrate is usual. Rapid-sequence induction with fentanyl, thiopentone, and suxamethonium is followed by inserting a right-sided endobronchial tube. Anesthesia is maintained with enflurane in oxygen and nitrous oxide and neuromuscular blockade with pancuronium [35]. On the other hand, delaying a decision to insert a double-lumen tube may have advantages. First, it may not be necessary if a simple laparotomy suffices; placing double-lumen tubes is often difficult, especially during rapid-sequence induction. Second, changing tubes intraoperatively allows surgical manipulation of the stomach directly, combined with a nasogastric tube, to ensure the abdominal stomach is empty before a double-lumen tube placement. Head-up tilt also reduces the risk of regurgitation from the abdominal or thoracic stomach [35].

Normal changes of pregnancy include increased cardiac output, which reaches its highest value after delivery due to blood transfer from the uterus into the systemic circulation and vena-caval compression release [36]. Diaphragmatic hernia is associated with intrathoracic pressure augmentation. It reduces venous return, increases right and left ventricular afterload, and decreases cardiac output. Thus, perioperative hemodynamic monitoring of patients with diaphragmatic hernia could improve fluid management. Although a pulmonary artery catheter is an invasive procedure, it is a gold standard for measuring cardiac output and pressures directly [37].

### 2.1.2.2 Abdominal Trauma

The literature on pregnant trauma victims' obstetric, anesthetic, and surgical management is limited [38]. Pregnant trauma victims present a unique spectrum of challenges to the trauma healthcare team. The diagnosis may be unknown at exploration, as may be the nature and extent of the further procedures. Pregnancy may not always be known to the healthcare team (at the scene of transportation accidents, emergency room, or operating room), complicating the situation.

Pregnancy must always be suspected (until proven otherwise) in female trauma patients of childbearing age [38].

Vasopressors, rarely indicated in trauma patients, should be avoided unless necessary because of the risk of decreasing uterine blood flow.

If vasopressors are required, ephedrine should be the first choice. It preserves the uterine blood flow, but there should be no hesitation in using other vasopressors when necessary.

### Head and Neck Injury

Women in late pregnancy have difficult airways. Mallampati class 4 airway (with only the hard palate visible and with no view of the soft palate or uvula) increased by 34% between 12 and 38 weeks [39]. The additional fact that these patients have sustained trauma and will likely be in cervical collars compounds is an already difficult situation [40]. If there is uncertainty about the integrity of the cervical spine, direct laryngoscopy should be avoided, and fiberoptic (awake fiberoptic) intubation of the trachea, if feasible (time constraints or equipment availability), should be considered [41]. If direct laryngoscopy is deemed necessary, an "inline stabilization" of the head and neck by an assistant to prevent extension and rotation of the cervical spine is indicated. If awake, fiberoptic tracheal intubation is chosen. Analgesic and sedative drug titration maintains continual meaningful verbal communication between the anesthesiologist and the patient.

Respiratory depression and aspiration of stomach contents with local anesthesia are less likely if the patient remains awake and alert. Also, a rational, alert mother minimizes the risk of neonatal depression. In patients in anesthesia, nasogastric decompression after intubation reduces the risk of aspiration. Midazolam is the recommended benzodiazepine. However, it is highly unionized and lipophilic, and the feto-maternal ratio is 0.76 at 15–20 min after maternal administration. However, unlike other benzodiazepines, the ratio falls rapidly. No adverse fetal effects have been reported [42]. Trauma victims with a GCS  $\leq$  8

usually require intubation and mechanical ventilation for intracranial pressure and airway control. However, trauma victims with “good” GCS can “talk and deteriorate/die” following a traumatic head injury, particularly an injury associated with loss of consciousness. Delayed deterioration occurs within 48 h from the initial insult.

The succinylcholine-induced ICP increase has been a concern in the past. With an urgent need to secure an airway in a head-injured pregnant trauma victim, succinylcholine is an appropriate and safe drug. All the intravenous anesthetic agents (except ketamine) cause some degree of vasoconstriction and therefore decrease cerebral blood flow. The inhaled agents have some cerebral vasodilatory effect; however, their administration is usually consistent with acceptable ICP levels [43].

### Spinal Cord Injury

The anesthetic management of a spinal cord injury in pregnancy depends upon the lesion’s site, extent, and duration. Complete cord transection is usually associated with cardiovascular instability due to neurogenic shock in the acute phase or subsequent autonomic hyperreflexia. In the latter case, epidural analgesia blocks afferent pathways, reducing the stimuli and causing paroxysmal sympathetic activity. Parasympathetic pathways are intact, and life-threatening bradycardia can occur. Intravascular volume status can be difficult to assess and manage, particularly in acute injury. Intravenous fluid therapy is best guided by central venous pressure monitoring. Attention to the patient’s position and the compression of pelvic venous structures by the gravid uterus distinguish between postural hypotension and volume depletion. Maternal hypotension must be avoided to maintain uterine blood flow and avoid secondary ischemic damage in the evolving cord lesion. Irrespective of the chosen method of anesthesia, preoperative and postoperative neurological findings should be documented.

If radiological evidence suggests that the neurological deficit is caused by edema, the principal anesthetic concern was to avoid secondary (irreversible) cord damage in the mother and enable timely delivery in case of

acute fetal compromise. If the patient has a normal airway and, other than the cervical collar, there are no reasons for anticipating difficulties with intubation, general anesthesia with inline neck stabilization during intubation is the most appropriate [44].

### 2.1.2.3 Increased Intra-Abdominal Pressure

Increased IAP (see Chap. 3) is transmitted to the thoracic cage (on average 50%), which diminishes lung compliance, decreases functional residual capacity, and increases ventilation/perfusion mismatch [45]. In critically ill pregnant women, abdominal compartment syndrome manifests in several ways. Ventilation becomes increasingly difficult, resulting in increased peak and plateau alveolar pressures, hypercapnia, hypoxia, and increased risk of ventilator-associated lung injury because of the high pressures needed to drive ventilation [46].

### 2.1.2.4 Acute Appendicitis

Pregnant patients with AA, compared to non-pregnant, have similar occurrences of all specific complications except pneumonia, which occurred more frequently in pregnant women (0.7% vs. 0.2%,  $p = 0.004$ ). All cases of postoperative pneumonia were observed in women who underwent general endotracheal anesthesia [47].

### 2.1.2.5 Uterine Rupture

With a UR diagnosis, the mother’s immediate stabilization and delivery of the fetus are imperative. After securing the airway and adequate oxygen delivery, careful and immediate correction of hypovolemia is mandatory. Patients should have multiple, preferably large-bore, intravenous catheters with vigorous fluid resuscitation. With complete and extensive UR with fetal extrusion into the peritoneal cavity and vaginal bleeding, ergometrine may be administered to control bleeding from the rent and the placental site during preparation for laparotomy.

The use of prophylactic antibiotics is controversial. Some state that they have no value [48], while others recommend their use [49] because 23% had intraperitoneal sepsis at the time of



laparotomy [50]. Partly it depends on the quantity of blood loss. Hypovolemic shock may lead to the translocation of gram-negative bacteria from the ischemic bowel to the bloodstream, complicating the presentation with endotoxemia and septic shock [51]. Hemorrhagic shock increases the incidence of wound infections. Most survived mothers had a mean blood loss of >2000 mL [52–54]. Blood loss depends on the trimester of UR and uterotonics or prostaglandins for labor induction. These medications can decrease the amount of blood loss [55].

At least 1000 mL of packed red blood cells or blood transfusions should be available [53, 54, 56].

### 2.1.3 Intraoperative CO<sub>2</sub> Monitoring

*During laparoscopy, intraoperative CO<sub>2</sub> monitoring by capnography should be used in the pregnant patient*

(Level III).

Fetal acidosis with insufflation has not been documented in the human fetus, but concerns over the potentially detrimental effects of acidosis have led to the recommendation of maternal CO<sub>2</sub> monitoring [57, 58]. Initially, there was a debate over maternal blood gas monitoring of arterial carbon dioxide (PaCO<sub>2</sub>) versus end-tidal carbon dioxide (ETCO<sub>2</sub>) monitoring. However, the less invasive capnography adequately reflects maternal acid-base status in humans [59]. The safety and efficacy of ETCO<sub>2</sub> measurements in pregnant women [60–62] make routine blood gas monitoring unnecessary.

### 2.1.4 Extracorporeal Membranous Oxygenation

#### 2.1.4.1 Considerations in Pregnancy

Extracorporeal membranous oxygenation (ECMO) is the last resuscitation treatment for patients with refractory shock. It is a complex

technique for providing life support in severe but potentially reversible respiratory failure. The technique oxygenates the blood outside the body, obviating the need for gas exchange in the lungs and, if necessary, provides cardiovascular support. General indications for ECMO are:

- Severe acute respiratory failure with an expected mortality rate of 80% based on physiological variables,
- Reversible respiratory failure,
- Spontaneous circulation not returning because of cardiac arrest or refractory ventricular fibrillation after 10 min CPR,
- Systolic blood pressure cannot be maintained at >70 mmHg and inotropic score (IS) >60 µg/kg/min, and intra-aortic balloon pump support (IS, µg/kg/min = dopamine + dobutamine + 15 × milrinone + 100 × epinephrine + 100 × norepinephrine + 100 × isoproterenol).

ECMO therapy may be beneficial during pregnancy or early puerperium in H<sub>1</sub>N<sub>1</sub>-related hypoxemia [63, 64], ARDS from various causes [65], and peripartum cardiomyopathy [66]. Venovenous ECMO is indicated for hypoxemic respiratory failure, hypercarbic respiratory failure, respiratory failure in lung transplant, bronchopleural fistulas, pulmonary air leaks, or complex airway management. In venovenous ECMO, no cardiac support is provided, as opposed to venoarterial extracorporeal membrane oxygenation [65].

#### 2.1.4.2 Amniotic Fluid Embolism

See Sect. 25.3.6.6. A total of 20 ECMO cases of amniotic fluid embolism from 1986 to 2019 were published [67]. Extracorporeal therapies consisted of venoarterial ECMO (11 cases), venovenous ECMO (3 cases), and cardiopulmonary bypass (3 cases, including 2 older cases). Extracorporeal therapies were started after delivery and were continued for a median of 48 h. The length of ICU stay ranged from 7 to 59 days. Maternal and neonatal survival was 85%. Maternal hemorrhage complicated 69% of cases, with a few patients requiring more than 10 red blood cell transfusions [67].

Although not strongly recommended, from 2020, ECMO for amniotic fluid embolism is included in the treatment guidelines— “persistent hemodynamic instability despite medical management or need for prolonged CPR may require consideration for VA ECMO” [68]. Postpartum hemorrhage or DIC should not be considered absolute contraindication [67].

#### 2.1.4.3 Maternal Trauma

A single case of successful ECMO therapy for maternal chest trauma has been reported [69].

## 2.2 Perioperative Medications

Interests of both the mother and the fetus must be considered in therapy during pregnancy. Usually, these interests do not conflict because what is good for the mother is generally good for the fetus. Sometimes maternal therapy must be modified to substitute alternative but safer therapy because of the concerns about drug teratogenicity (e.g., replacing a H<sub>2</sub> receptor antagonist for misoprostol, an abortifacient that is contraindicated during pregnancy) [70, 71]. Rarely, the maternal and fetal interests are opposed, as in chemotherapy for maternal cancer. This therapy is potentially life-saving to the mother but life-threatening to the fetus [72]. These conflicts raise significant medical, legal, and ethical issues.

There are many categories of drugs that could have deleterious effects on a fetus, and detailed elaboration is out of the scope of this book. There are three main categories of medications used in these patients: (1) anesthetic medications (see Sect. 2.1.1), (2) prophylactic, and (3) therapeutic. All teratogenic drugs generally determine a specific pattern or single malformation during a sensitive gestation period with a dose-dependent effect.

### 2.2.1 Antibiotics

The US Food and Drug Administration has categorized all antibiotics according to the risks associated with their use in pregnancy. Two categories are important:

- category A: studies in pregnant women do not demonstrate any risks to the mother or fetus,
- category B: while animal studies show no risk, human studies are inadequate, or animal toxicity has been noted, but the studies on humans show no risk.

There are no antibiotics in category A. FDA Class B antibiotics should be administered when the acute abdomen is highly suspected or found (at least 30–60 min before skin incision) in all patients (administered to 94% of patients in the literature) [73].

#### 2.2.1.1 Acute Appendicitis

Recommended antibiotics are second-generation cephalosporins (FDA Class B), comprising 60% of all antibiotic classes used during pregnancy for acute appendicitis (AA) [74]. Cephalosporins and metronidazole are indicated for gangrenous or perforated AA [75]. Metronidazole use in pregnant patients is still controversial, with a recommendation against its use during the first trimester of pregnancy. However, there is no increase in teratogenic risk when used in recommended doses regardless of the trimester [76, 77]. The duration of antibiotic therapy should be discontinued as early as possible. A single preoperative dose is adequate with normal appendix or phlegmonous AA [78]. Even operation without antibiotic therapy for phlegmonous AA is sufficient in the nonpregnant population. Therefore, for a pregnant patient with high suspicion of AA, the time from admission to the operation should be short as possible.

#### 2.2.1.2 Acute Cholecystitis

Penicillins and second-generation cephalosporins are most commonly used. The first-line treatments are ampicillin and sulbactam or cefoxitin/cefuroxime. There is no consensus on the duration of antibiotic use in pregnancy. Recommendations from the general population can be applied: (1) to use antibiotics until the patient becomes afebrile and without leukocytosis or elevated CRP, or (2) single dose or 24-h therapy in organ occupying infection [78].

## 2.2.2 Pain Management

### 2.2.2.1 NSAIDs

The use of NSAIDs during the second and third trimesters is associated with oligohydramnios and anuria. After 30 weeks of gestation, it is associated with an increased risk of premature closure of the fetal ductus arteriosus (Botalli's duct), with subsequent pulmonary hypertension, intracranial hemorrhage, and necrotizing enterocolitis [79–84]. After appendectomy with CS, all classes of medications could be used as in nonpregnant patients unless contraindicated for maternal reasons.

NSAIDs were the first-choice treatment for symptomatic relief, but the risk of miscarriage was the highest with NSAID use around conception and increased with NSAID use for longer than a week [85–87]. Prostaglandins are needed to successfully implant an embryo into the uterus wall [88] and play an important role in human ovulation and implantation through their effect and interaction with platelet-activating factors and cytokines, both in the uterus and in the embryo [89, 90]. Suppression of prostaglandin biosynthesis by NSAIDs could lead to abnormal implantation with a predisposition for miscarriage [87]. There are also differences in transplacental pharmacokinetic parameters between different NSAIDs. The results suggest that the fetal risk of diclofenac is higher than salicylic acid and antipyrine [91]. If indicated, ibuprofen is the preferred agent. Unfortunately, selective NSAIDs (cyclo-oxygenase 2 inhibitors) are classified in FDA category C because of increased peri-implantation and postimplantation losses and reduced fetal survival in rats and rabbits.

NSAIDs and aspirin should be given in pregnancy only if the maternal benefits outweigh the potential fetal risks, at the lowest effective dose, and for the shortest duration (less than a week) with avoidance during conception and ideally after 30 weeks of pregnancy.

### 2.2.2.2 Paracetamol

Paracetamol, which shares many indications with NSAIDs, did not affect the risk of miscarriage. NSAIDs and aspirin inhibit prostaglandin biosynthesis in most organ systems, whereas paracetamol inhibits prostaglandin biosynthesis only in the central nervous system [86].

During pregnancy, paracetamol is the drug of choice for analgesic, anti-inflammatory, and antipyretic action.

### 2.2.2.3 Opioids

Weak opioids such as codeine may be used as additional treatments to help control the pain. They are also helpful if NSAIDs are not tolerated or are contraindicated. Morphine analgesia and its derivatives should be avoided, as they may cause spasms of the sphincter of Oddi. This spasm may exacerbate an already painful acute cholecystitis or biliary obstruction.

### 2.2.2.4 Local Anesthesia

Long-acting local anesthesia utilized in laparoscopic port sites or laparotomy wound improves postoperative analgesia, minimizing postoperative narcotic requirements.

## 2.2.3 Thromboprophylaxis and Anticoagulation

### 2.2.3.1 General Recommendations

The annual frequency of deep venous thrombosis (DVT) in the general population is 0.16–1% [92, 93], of which 2% are pregnancy-related [94]. Therefore, the risk of a thromboembolic event, either DVT or pulmonary embolism (PE), during pregnancy and puerperium is estimated to be tenfold higher, reaching 2% [92, 95–98]. Gestational hormones, particularly estrogen, contribute to mild hypercoagulability during pregnancy by increasing the synthesis of clotting factors [99]. Thromboembolic phenomena are also promoted by intra-abdominal vascular stasis resulting from

**Table 2.4** Risk factors for thrombosis during pregnancy [92, 93, 95, 96, 101]

| Thrombophilic disorders                         | Causes related to pregnancy          | General risk factors                |
|-------------------------------------------------|--------------------------------------|-------------------------------------|
| Antithrombin deficiency                         | Immobility                           | Age >35 years                       |
| Factor V Leiden                                 | Parity $\geq 3$                      | Body mass index >30                 |
| Antiphospholipid Antibodies                     | Multiple gestations                  | History of deep vein thrombosis     |
| Hyperhomocysteinemia                            | Weight gain >21 kg                   | Smoking                             |
| Protein C deficiency                            |                                      | Diabetes mellitus                   |
| Homozygous MTHFR C677T                          | Prolonged labor >12 h                | Major abdominal surgery for >30 min |
| Protein S deficiency                            | Preeclampsia                         |                                     |
| Prothrombin gene Mutation                       | (emergency) cesarean section         | Anemia                              |
| Plasminogen activator Inhibitor-1 (PAI-1) 4G/5G | Blood loss (>1 l)/ blood transfusion | Black race                          |
|                                                 | Preterm delivery                     | Dehydration                         |
|                                                 | Mid-cavity instrumental delivery     | Infections                          |
|                                                 | Hyperemesis                          | Severe varicose veins               |
|                                                 | Assisted reproductive techniques     | Systemic lupus erythematosus        |

compression by the enlarged gravid uterus. The risk may increase exponentially throughout the pregnancy [100]. Puerperium is the period with the highest venous thromboembolism (VTE) risk, up to 25-fold higher than that in nonpregnant women [92, 96, 98, 101]. Around 43–60% of pregnancy-related PE episodes occur during puerperium [92, 95]. Approximately 80% of thrombotic events occur in the first 3–4 weeks after delivery and are explained by the immobility and the trauma of pelvic vessels at delivery, leading to endothelial damage [102].

Hypercoagulability during the obstetric period is explained by many factors, including abnormalities in coagulation proteins (increased levels of factors II, V, VII, VIII, X, XII, and von Willebrand factor, and decreased levels of protein S and activated protein C) and abnormalities in the fibrinolytic system (low plasma fibrinolytic activity during pregnancy, labor, and delivery) with decreased activity of tissue plasminogen activator. The most significant changes occur in factor VIII and fibrinogen levels, each of which increases two to threefold [103, 104].

*Pregnant women undergoing nonobstetric surgery should be screened for venous thromboembolism risk and should have the appropriate perioperative prophylaxis administered. (ACOG Committee opinion 2019 [1])*

Risk factors for thrombosis during pregnancy are listed in Table 2.4. The American College of Chest Physicians Evidence-Based Clinical Practice Guidelines 2012 is the most comprehensive thromboprophylaxis guideline for the pregnant population [97].

- Low-molecular-weight heparin (LMWH) is recommended for the prevention and treatment of VTE instead of unfractionated heparin (UFH),
- For women receiving anticoagulation for the treatment of VTE who become pregnant, LMWH is recommended over vitamin K antagonists,
- The use of fondaparinux and parenteral direct thrombin inhibitors should be limited to those with severe allergic reactions to heparin (e.g., HIT) who cannot receive danaparoid,
- Avoid the use of oral direct thrombin (e.g., dabigatran) and anti-Xa (e.g., rivaroxaban, apixaban) inhibitors,
- For lactating women using warfarin, acenocoumarol, or UFH who wish to breastfeed, continuing the use of warfarin, acenocoumarol, or UFH is recommended,

- For lactating women using LMWH, danaparoid, or r-hirudin who wish to breastfeed, a continuation of LMWH, danaparoid, or r-hirudin is recommended,
- For breastfeeding women, alternative anticoagulants rather than fondaparinux are recommended,
- For breastfeeding women, alternative anticoagulants rather than oral direct thrombin (e.g., dabigatran) and factor Xa inhibitors (e.g., rivaroxaban, apixaban) are recommended,
- For lactating women using low-dose aspirin for vascular indications who wish to breastfeed, a continuation of this medication is recommended,
- For women undergoing assisted reproduction, routine thrombosis prophylaxis is not recommended,
- For women undergoing assisted reproduction who develop severe ovarian hyperstimulation syndrome, thrombosis prophylaxis (prophylactic LMWH) for 3 months postresolution of clinical ovarian hyperstimulation syndrome is recommended,
- For all pregnant women with prior VTE, postpartum prophylaxis for 6 weeks with prophylactic- or intermediate-dose LMWH or vitamin K antagonists targeted at INR 2.0-3.0 is recommended,
- For pregnant women at low risk of recurrent VTE (a single episode of VTE associated with a transient risk factor not related to pregnancy or use of estrogen), only clinical vigilance antepartum is recommended,
- For pregnant women at moderate to high risk of recurrent VTE (single unprovoked VTE, pregnancy- or estrogen-related VTE, or multiple prior unprovoked VTE not receiving long-term anticoagulation), antepartum prophylaxis with prophylactic- or intermediate-dose LMWH is recommended,
- For pregnant women receiving long-term vitamin K antagonists, an adjusted dose of LMWH or 75% of a therapeutic dose of LMWH throughout pregnancy followed by resumption of long-term anticoagulants postpartum is recommended,
- For pregnant women with no prior history of VTE who are known to be homozygous for factor V Leiden or the prothrombin 20210A mutation and have a positive family history of VTE, antepartum prophylaxis with prophylactic- or intermediate-dose LMWH and postpartum prophylaxis for 6 weeks with prophylactic- or intermediate-dose LMWH or vitamin K antagonists targeted at INR 2.0-3.0 is recommended,
- For pregnant women with all other thrombophilias and no prior VTE who have a positive family history of VTE, antepartum clinical vigilance and postpartum prophylaxis with prophylactic- or intermediate-dose LMWH or, in women who are not protein C or S deficient, vitamin K antagonists targeted at INR 2.0-3.0 are recommended,
- For pregnant women with no prior history of VTE who are known to be homozygous for factor V Leiden or the prothrombin 20210A mutation and who do not have a positive family history of VTE, antepartum clinical vigilance and postpartum prophylaxis for 6 weeks with prophylactic- or intermediate-dose LMWH or vitamin K antagonists targeted at INR 2.0-3.0 are recommended,
- For pregnant women with all other thrombophilias and no prior VTE who do not have a positive family history for VTE, antepartum and postpartum clinical vigilance are recommended,
- For women with recurrent early pregnancy loss (three or more miscarriages before 10 weeks of gestation), screening for APLAs is recommended,



- For women with a history of pregnancy complications, no screening for inherited thrombophilia is recommended,
- For women who fulfill the laboratory criteria for APLA syndrome and meet the clinical APLA criteria based on a history of three or more pregnancy losses, antepartum administration of prophylactic- or intermediate-dose UFH or prophylactic LMWH combined with low-dose aspirin, 75–100 mg/d is recommended,
- For women with inherited thrombophilia and a history of pregnancy complications, antithrombotic prophylaxis is not recommended,
- For women considered at risk for preeclampsia, low-dose aspirin throughout pregnancy, starting from the second trimester, is recommended,
- For women with two or more miscarriages but without APLA or thrombophilia, antithrombotic prophylaxis is not recommended,
- For pregnant women with mechanical heart valves: (a) adjusted-dose bid LMWH throughout pregnancy to achieve the manufacturer's peak anti-Xa LMWH 4 h postsubcutaneous injection, or (b) adjusted-dose UFH throughout pregnancy administered subcutaneously every 12 h in doses adjusted to keep the mid-interval aPTT at least twice control or attain an anti-Xa heparin level of 0.35–0.70 units/mL, or (c) UFH or LMWH (as above) until the 13th week, with substitution by vitamin K antagonists until close to delivery when UFH or LMWH is resumed.

### 2.2.3.2 Low-Risk Surgery

Many factors can alter postoperative coagulation. These include the type of operation [105] and anesthesia [106]. Postoperative changes in cytokine levels are affected by even more factors: the

type of the procedure and the anesthetic technique or anesthetic agent [107], the duration of the operation [108], and the use of autologous or allogenic transfusion [109].

Open surgery (OS), compared with laparoscopic surgery (LS), leads to activation of the clotting system to a higher degree, implying a greater thromboembolic risk. Subclinical fibrinolysis is also more profound with OS. Although of a lower degree, hypercoagulability is observed in patients undergoing LS. This fact, combined with the pneumoperitoneum-induced venous stasis of the legs, explains the reduced, but not negligible, rate of thromboembolic complications after LS. Therefore, routine thromboembolic prophylaxis (subcutaneous LMWH, elastic compression stockings, intraoperative pneumatic stockings, and early postoperative patient mobilization) should be considered for LS [110]. Gestational hormones, particularly estrogen, contribute to mild hypercoagulopathy during pregnancy by increasing the synthesis of clotting factors [99]. If a laparotomy can be avoided, recovery time is greatly reduced; thus, postoperative complications due to immobilization, such as DVT and PE, are less likely. Prophylaxis with pneumatic compression devices, both intraoperatively and postoperatively, and early postoperative ambulation are recommended.

No recommendations for thromboprophylaxis exist for low-risk groups (appendectomy via laparoscopy or gridiron incision, isolated Fallopian tube torsion, and (ruptured) ectopic pregnancy). The use of calf-length sequential pneumatic compression stockings increases venous return and prevents the risk of VTE [111]. Early ambulation further minimizes or eliminates the VTE risk.

### 2.2.3.3 Elective Cholecystectomy

A marked hypercoagulable state after LC is seen by an increase in the thromboelastographic index on the first postoperative day compared to preoperative values [105]. Reports have documented a reduction in postoperative hypercoagulability after LS compared to OS [112, 113]. A significant increase in prothrombin fragment F1 + 2 levels after LC is found, but these levels were significantly lower than those after OC [113]. Conversely, others have not found a difference in

postoperative hemostasis between LC and OC [114, 115]. Fibrinogen levels increased and reached maximum levels at 72 h, but significantly less after LC than after OC. In contrast, plasminogen levels decreased postoperatively without a significant difference between groups [116]. LC is associated with a lesser degree of thromboembolic complications despite pneumoperitoneum, which, by reducing venous inflow toward the heart, promotes venous stasis of the legs and predisposes to DVT [117, 118]. TAT, F1, FIB, soluble fibrin, and D-dimer plasma levels until 72 h after surgery were significantly higher in the OC group than in the LC group, implying significantly higher activation of coagulation and fibrinolysis in the OC group [116]. The levels of coagulation factors and cytokines were, on average, two times higher in the OC group. Other nonrandomized studies found insignificant differences in fibrinolytic activity between OC and LC groups [114, 115, 119]. Postoperative DVT is additionally reduced after LC due to the early mobility of such patients.

#### 2.2.3.4 Emergent Cholecystectomy

The emergent LC carries a better fetal prognosis than delayed cholecystectomy (see Sect. 16.1.8.4). Still, there are several issues. First is coagulation and fibrinolysis mechanisms during pregnancy complicated with acute cholecystitis. Second is the question of coagulation during the complete process of cholecystitis as a disease. Is it better to perform emergent cholecystectomy with initially increased coagulation or to start medical management, which, due to inflammation, also increases coagulation? Moreover, coagulation is also increased in the second phase of the treatment process when delayed elective cholecystectomy is performed. There are no recommendations for additional thromboprophylaxis in acute cholecystitis during pregnancy.

#### IVF Pregnancy

Currently, there is only one case report of LC due to acute cholecystitis during pregnancy [99]. Thromboprophylaxis should be recommended in dosage for IVF pregnancy due to its higher risk for VTE. Prospective studies should solve this issue.

#### 2.2.3.5 General IBD Patients (ECCO Consensus)

IBD patients in general, particularly those hospitalized with the active disease, are at increased risk for VTE [120, 121]. Hospitalized pregnant IBD patients have an increased risk of VTE compared to non-IBD pregnant controls, for CD an OR 6.12 and UC an OR 8.44. LMWH in a prophylactic dose reduces VTE risk in medical and surgical patients by 60–70%.

LMWH is safe and effective in the pregnant population [122]. Therefore, prophylactic LMWH in pregnant IBD patients experiencing a relapse or being admitted to the hospital is recommended. Women should undergo a documented assessment of risk factors for VTE in early pregnancy or before pregnancy. This assessment should be repeated if the woman is admitted to the hospital and again after delivery.

Pregnant women with IBD are at increased risk of vitamin D insufficiency compared with those without IBD. The current guidelines for vitamin D supplementation (400 IU/day) may be inadequate for pregnant women with IBD [123].

#### 2.2.3.6 Cesarean Section

The VTE incidence rate following CS is 1.78%, with an odds ratio of 2 [95]. Thromboprophylaxis guidelines from the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines 2012 for women undergoing CS are presented [97]:

- For women undergoing CS without additional thrombosis risk factors, thromboprophylaxis is not recommended other than early mobilization,
- For women at increased risk of VTE after CS because of the presence of one major or at least two minor risk factors, pharmacologic thromboprophylaxis (prophylactic LMWH) or mechanical prophylaxis (elastic stockings or intermittent pneumatic compression) in those with contraindications to antico-

agulants while in hospital following delivery is recommended,

- For women undergoing CS who are considered to be at very high risk for VTE and who have multiple additional risk factors for thromboembolism that persist in the puerperium, prophylactic LMWH should be combined with elastic stockings or intermittent pneumatic compression,
- For selected high-risk patients in whom significant risk factors persist following delivery, extended prophylaxis (up to 6 weeks after delivery) following discharge from the hospital is recommended.

- For pregnant women receiving adjusted-dose LMWH therapy and where delivery is planned, discontinuation of LMWH at least 24 h before induction of labor or CS (or expected time of neuraxial anesthesia) rather than continuing LMWH up until the time of delivery is recommended.

### 2.2.3.7 Torsion of the Gravid Uterus

Several cases of PE after uterine detorsion [124, 125] exist. Therefore, LMWH (enoxaparin 20 mg once a day) for 6 weeks to prevent VTE is recommended [126].

### 2.2.3.8 Venous Thromboembolism

Therapeutic recommendations for VTE during pregnancy from the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines 2012 are presented [97]:

- For pregnant women with acute VTE, adjusted-dose subcutaneous LMWH over adjusted-dose UFH is recommended,
- For pregnant women with acute VTE, LMWH over vitamin K antagonist treatment antenatally is recommended,
- For pregnant women with acute VTE, anticoagulants should be continued for at least 6 weeks postpartum (for a minimum total duration of therapy of 3 months),

### Mesenteric Vein Thrombosis

Guidelines for the duration of anticoagulation after pregnancy for mesenteric vein thrombosis (MVT) do not exist, and decisions on a case-by-case basis need to be taken by hematologists [127]. In the general population, anticoagulation with low-molecular-weight heparin should be initiated as soon as the diagnosis is made, including when the diagnosis is delayed until surgery [128]. Although maintenance anticoagulation therapy is recommended for at least 6 months after diagnosis to prevent the recurrence of the thrombosis, its benefit was questioned during pregnancy [129]. Lifelong anticoagulation is warranted with inherited hypercoagulable disorders (i.e., protein S, protein C, antithrombin III deficiencies, and factor V Leiden mutation). For a general population with reversible predisposing causes, at least 6 months of anticoagulation is recommended [130].

Guidelines for anticoagulation management strategies exist for various clinical situations before and after controlled ovarian stimulation [131, 132]. A history of prior MVT should be placed in the clinical classification of the previous episode(s) of venous thromboembolism receiving long-term anticoagulation. It is recommended to switch from oral anticoagulants to LMWH therapy (e.g., enoxaparin 1 mg/kg every 12 h) before controlled ovarian stimulation and continue throughout pregnancy [131, 132]. The recommendation is to refrain from administering LMWH for 24 h before egg retrieval and restart therapeutic anticoagulation



3 h after egg retrieval [131, 132]. Without large studies, IVF associated with MVT indicates lifelong oral anticoagulation in patients at low risk for bleeding and full anticoagulation with LMWH per the above protocol during repeat IVF cycles. However, controversy in preventing venous thrombosis exists after delivery, especially if no risk factors were detected [133]. Though the induction of oral anticoagulation in protein C deficiency has been widely used, it carries significant risks in patients with esophageal varices and thrombocytopenia [134].

## 2.3 Perioperative Management

*Surgery should be done at an institution with neonatal and pediatric services.*

(ACOG Committee opinion 2019 [1])

*An obstetric care provider with cesarean delivery privileges should be readily available.*

(ACOG Committee opinion 2019 [1])

### 2.3.1 Fetal Heart Rate Monitoring

*If the fetus is considered previable, it is generally sufficient to ascertain the fetal heart rate by Doppler before and after the procedure.*

(ACOG Committee opinion 2019 [1])

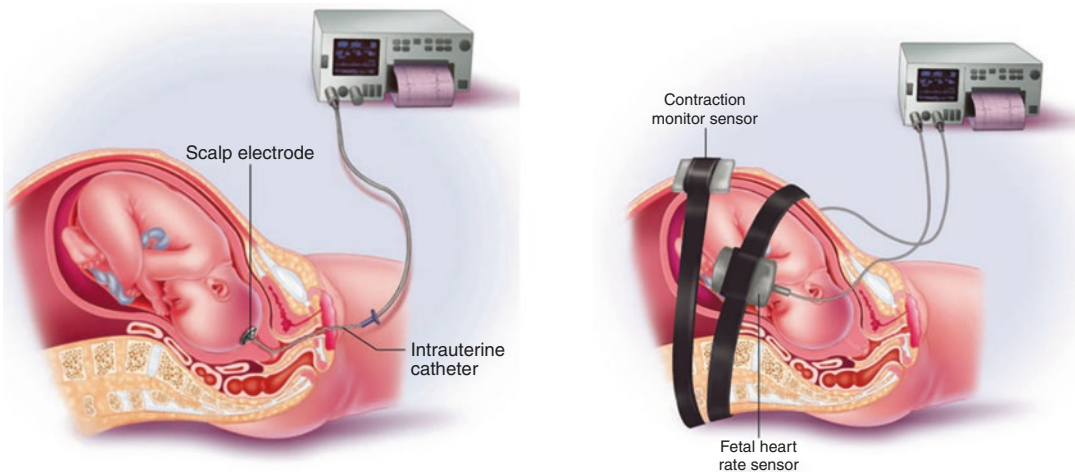
*At a minimum, if the fetus is considered to be viable, simultaneous electronic fetal heart rate and contraction monitoring should be performed before and after the procedure to assess fetal well-being and the absence of contractions.*

(ACOG Committee opinion 2019 [1])

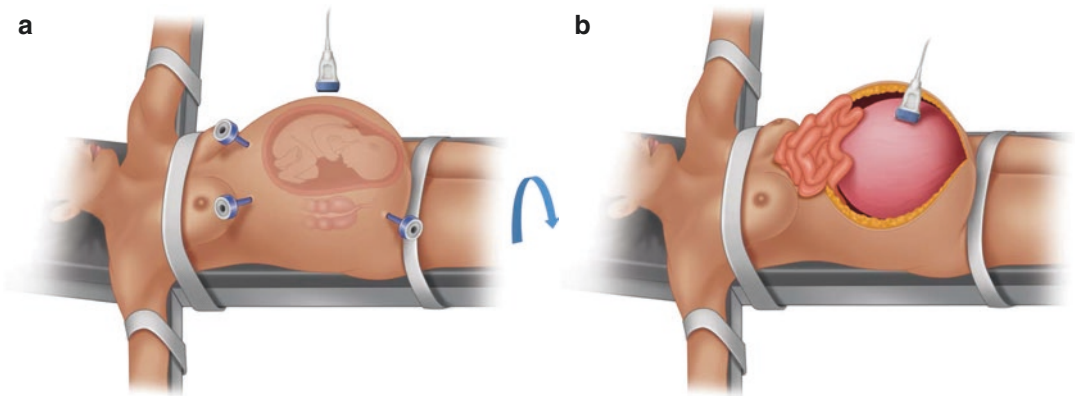
There are two principal types of FHR monitoring: internal and external (Fig. 2.2). When emergency abdominal conditions are considered, only the external type is used. FHR, after 16 weeks of pregnancy, should be monitored pre- and postoperatively in the setting of urgent

abdominal surgery during pregnancy (Evidence level III) [135, 136]. In specific circumstances, intraoperative electronic fetal monitoring can be appropriate but is never practiced in emergency abdominal surgery in pregnancy [1]. *Indirect* (transabdominal) intraoperative FHR (every 5 min in the lower left quadrant without disinflation) resembles external FHR monitoring (Fig. 2.3a) to detect fetal distress and is used during laparoscopy. No intraoperative FHR abnormalities have been reported [137, 138]. *Direct* (transuterine) FHR monitoring is performed during laparotomy (Fig. 2.3b). Three methods of intraoperative FHR monitoring include (1) cardiotocography, (2) ultrasonography with a transesophageal echocardiography probe, and (3) point-of-care ultrasound [139, 140]. One of the limitations of point-of-care ultrasound is that it cannot always serve as a continuous monitoring tool because of interference from the pneumoperitoneum. External monitors of uterine contractions are variably effective in the insufflated abdomen [141].

The effects of general anesthesia on cardiotocography result in a reduction of beat-to-beat variation with normal baseline frequency. The decreased variability can persist until 90 min in the postoperative course due to the residual effects of anesthetic agents on the fetus. Also, preoperative anxiety and stress can further increase catecholamine levels. This could be misinterpreted as fetal distress, leading to an emergency delivery and adding to fetal morbidity and mortality [143]. Additional factors that can influence intraoperative beat-to-beat variations are surgical manipulation, especially of the pregnant uterus, primary inflammatory process, or bleeding. Transvaginal sonography should be used during the procedure because the signals from transabdominal ultrasound would be lost during insufflation [144–146]. This has led some to recommend only pre-, and postoperative monitoring



**Fig. 2.2** Internal and external types of fetal heart rate monitoring. (Reproduced with permission from [142])



**Fig. 2.3** Intraoperative fetal monitoring. (a) Indirect during laparoscopy in advanced pregnancy. (b) Direct fetal monitoring during laparotomy

of the FHR as no increased fetal morbidity has been reported [60, 135].

Special monitoring precautions beyond those usually employed during general anesthesia—continuous maternal pulse oximetry, end-tidal  $\text{CO}_2$  monitoring, electrocardiography, and pulse rate measurements, combined with frequent blood pressure measurements—have generally not been employed. Also, in women predisposed to significant hypercarbia, changes in end-tidal  $\text{CO}_2$  may lag significantly behind maternal  $\text{PaCO}_2$ . Frequent direct measurements of maternal  $\text{PaCO}_2$  via an arterial catheter may be warranted [146].

Some faults of pneumoperitoneum can be avoided with the use of gasless laparoscopy.

There are fewer derangements in maternal and fetal physiology without  $\text{CO}_2$  pneumoperitoneum. Moreover, it is possible to perform surgical procedures under locoregional (peridural or spinal) rather than general anesthesia.

### 2.3.2 Perioperative Nutrition

#### 2.3.2.1 Total Parenteral Nutrition and Refeeding Syndrome

##### Pathophysiology

Refeeding syndrome was first recognized during World War II when returning prisoners of the Japanese who had been starved rapidly devel-

oped neurological and cardiovascular abnormalities after the institution of a normal diet [147]. The pathophysiology of refeeding syndrome relates to the rapid rise in insulin production following a carbohydrate or protein shock when protein calories are administered at a rate above which the patient can tolerate. This can occur in those receiving moderate dietary intake depending on their underlying nutritional, metabolic, or physical condition and may arise with glucose administration alone. This insulin release, associated with possible increased insulin sensitivity, leads to increased cellular uptake of glucose, fluid, and electrolytes with associated altered plasma availability of electrolytes.

Refeeding syndrome can manifest as either metabolic changes (hypokalemia, hypophosphatemia, hypomagnesemia, altered glucose metabolism, and fluid balance abnormalities) or physiological changes (i.e., arrhythmias, altered

level of consciousness, seizures, cardiac or respiratory depression) and potentially death [148].

### Total Parenteral Nutrition in Pregnancy

Total parenteral nutrition has been used successfully in pregnant women with hyperemesis gravidarum, postintestinal surgery, and acute pancreatitis [149]. The maternal and neonatal outcomes measured by adequate maternal weight gain and fetal growth are not compromised by total parenteral nutrition [150]. The average daily intake through total parenteral nutrition in pregnant women should be 2430 kcal [151]. However, it is better to increase daily calories to avoid refeeding syndrome.

Algorithms for initial management (Table 2.5) and monitoring (Table 2.6) of the refeeding syndrome from the *Drug Therapy Guideline No: 46.00 Issued: 10.10.07 Refeeding Syndrome Guideline (NHS trust)* are presented:

**Table 2.5** Initial management of refeeding syndrome

|                                                                                                                                                                                                                                                                                                                                |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Identification and Treatment of Sepsis                                                                                                                                                                                                                                                                                      |
| • May not be clinically apparent but may explain an acute deterioration                                                                                                                                                                                                                                                        |
| • Low threshold for septic screen                                                                                                                                                                                                                                                                                              |
| • Low threshold for broad-spectrum antibiotics (orally or via NG tube if possible)                                                                                                                                                                                                                                             |
| 2. Fluid Resuscitation and Monitoring Fluid Balance                                                                                                                                                                                                                                                                            |
| • Assess and carefully restore circulatory volume, monitor pulse rate, fluid intake, and output                                                                                                                                                                                                                                |
| • Malnourished patients have a reduced tolerance of intravenous fluids in moderate to high intakes (>2 L/24 h), which can lead to heart failure                                                                                                                                                                                |
| • Administration of intravenous fluids may be necessary for the initial 72 h until sufficient oral intake is achieved                                                                                                                                                                                                          |
| • Evidence of dehydration—for careful rehydration, i.e., 1–2 L in the first 24 h, depending on response. Greater volumes only if severely dehydrated                                                                                                                                                                           |
| • Total fluid intake (including intravenous, enteral, and oral) should aim for a maximum of 30 mL/kg per day ( $\leq 1.5$ L)                                                                                                                                                                                                   |
| • At least 6 hourly monitoring of blood pressure, pulse, and respiratory rate is necessary to detect evidence of heart failure or inadequate intravascular volume                                                                                                                                                              |
| 3. Correction of Electrolyte Abnormalities                                                                                                                                                                                                                                                                                     |
| • Ensure recent (last 48 h) electrolyte levels are available. These should include: urea and electrolytes, phosphate, calcium, magnesium (add to standard blood profile), liver function tests, full blood count                                                                                                               |
| • If electrolytes are deranged, consider and treat possible causes                                                                                                                                                                                                                                                             |
| • Perform ECG if Potassium is less than 3.5 mmol/L or Phosphate is less than 0.80 mmol/L                                                                                                                                                                                                                                       |
| • Organize supplementation if: Phosphate <0.8 mmol/L, K <3.5 mmol/L, Mg <0.5 mmol/L or adjusted Ca <2.0 mmol/L                                                                                                                                                                                                                 |
| • Caution should be used in renal patients due to the reduced excretion of these electrolytes                                                                                                                                                                                                                                  |
| • If very low plasma electrolyte values are demonstrated, e.g., Phosphate <0.32 mmol/L                                                                                                                                                                                                                                         |
| • K <2.5 mmol/L, Mg <0.5 mmol/L, then the institution of feeding or nutritional support may result in a further drop of these electrolytes to possibly critical levels. Electrolyte correction with oral or intravenous supplementation is required to achieve levels above these thresholds before the institution of feeding |

**Table 2.5** (continued)

|                                                                                                                                                                                                                                             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 4. Correction of Hypoglycemia/Blood Sugar Control                                                                                                                                                                                           |
| • Monitor blood glucose once to twice daily unless more frequent tests are indicated (i.e., for those patients with known diabetes or IGT)                                                                                                  |
| • If hypoglycemic, replace IV fluids with 5% glucose                                                                                                                                                                                        |
| 5. Management of Hypothermia                                                                                                                                                                                                                |
| • Monitor body temperature and, if necessary, the core temperature at least daily                                                                                                                                                           |
| • Hypothermia is commonly associated with malnutrition. Its correction should be simultaneous with fluid rehydration and can include the provision of heated drinks and blankets                                                            |
| 6. Correction/Prevention of Micronutrient Deficiencies                                                                                                                                                                                      |
| • Administer Thiamine 100 mg orally or crushed via feeding tube three times daily for 10 days or until recommended feeding rate is reached, with the first dose being administered at least 30 min before instituting feeding               |
| • If an enteral route is not available, the patient has anorexia nervosa or has chronic alcoholism; administer Pabrinex IVHP—1 pair of ampoules 30 minutes before instituting feeding and then daily until recommended feeding rate reached |
| • Administer vitamin B compound strong (one tablet three times daily) and Sanatogen Gold (one tablet daily) orally or crushed via a feeding tube                                                                                            |

**Table 2.6** Monitoring of patients with suspected or proven refeeding syndrome (minimum 72 h)

|                                                                                                                                                                                                                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Monitor until levels are in the reference range or the patient is on a stable feeding regimen:                                                                                                                     |
| • Serum urea and electrolytes, adjusted calcium, phosphate, and liver function tests at least daily                                                                                                                |
| • Serum magnesium; baseline, every 3 days and then weekly once stable                                                                                                                                              |
| • Fluid balance daily                                                                                                                                                                                              |
| • Blood glucose once to twice daily unless more frequent tests are indicated                                                                                                                                       |
| • Temperature, pulse, respiration, heart rate; daily                                                                                                                                                               |
| • Blood pressure 6 hourly                                                                                                                                                                                          |
| • ECG if abnormal heart rate or pulse. The patient will require cardiac monitoring if there is evidence of cardiac abnormalities on assessment or during refeeding. If necessary, transfer to the appropriate ward |
| <b>Clinical deterioration may reflect rapid overfeeding. Too little is always safer than too much, half the rate of feeding and observe</b>                                                                        |

Early parenteral nutrition in Crohn’s disease maintains normal maternal metabolism and normal fetal development in patients with the operation and complicated perioperative courses. Early parenteral nutrition should be considered in acute pancreatitis due to a protracted course with disease flares.

**2.3.2.2 Perinatal Outcome**

Symptomatic cholelithiasis or cholecystitis in pregnant women could be associated with a

higher risk of neonatal neural tube defects [152]. Confounding factors for preterm labor should be considered. An association exists between neural tube defects or other congenital anomalies and high fever during the critical period [153]. The hypothesis for the association between symptomatic cholelithiasis or cholecystitis and neural tube defects is based on a frequently present fever. It is a single factor that may play a role in the origin of neural tube defects (see Sect. 4.7.3). Thus, periconceptional folic acid/multivitamin supplementation in pregnant women with symptomatic cholelithiasis or cholecystitis is recommended [152, 153] and other abdominal conditions when the caloric intake is diminished. Folic acid and folic acid-containing multivitamins were less frequent in the symptomatic cholelithiasis or cholecystitis group, partly due to a higher rate of anorexia or vomiting. No association between the bacterial causes of cholecystitis and neural tube defects has been proven [154]. The drugs used to treat symptomatic cholelithiasis or cholecystitis have no role in the origin of neural tube defects. Recommended prenatal vitamin supplementation is based on the inverse relationship of the B vitamins (i.e., folate, vitamins B1, B2, B6, and B12), minerals, and vitamin E with CDH in newborns [155].

Dietary supplementation of  $\omega$ -3 has been suggested as secondary prevention of all-cause spontaneous preterm delivery, implying that  $\omega$ -3 fatty

acids can prolong the duration of gestation by 4–7 days and that dietary intake is marginal in Western populations [156]. A dose-response relation reflects an intake of up to 0.15 g  $\omega$ -3 fatty acids [157].

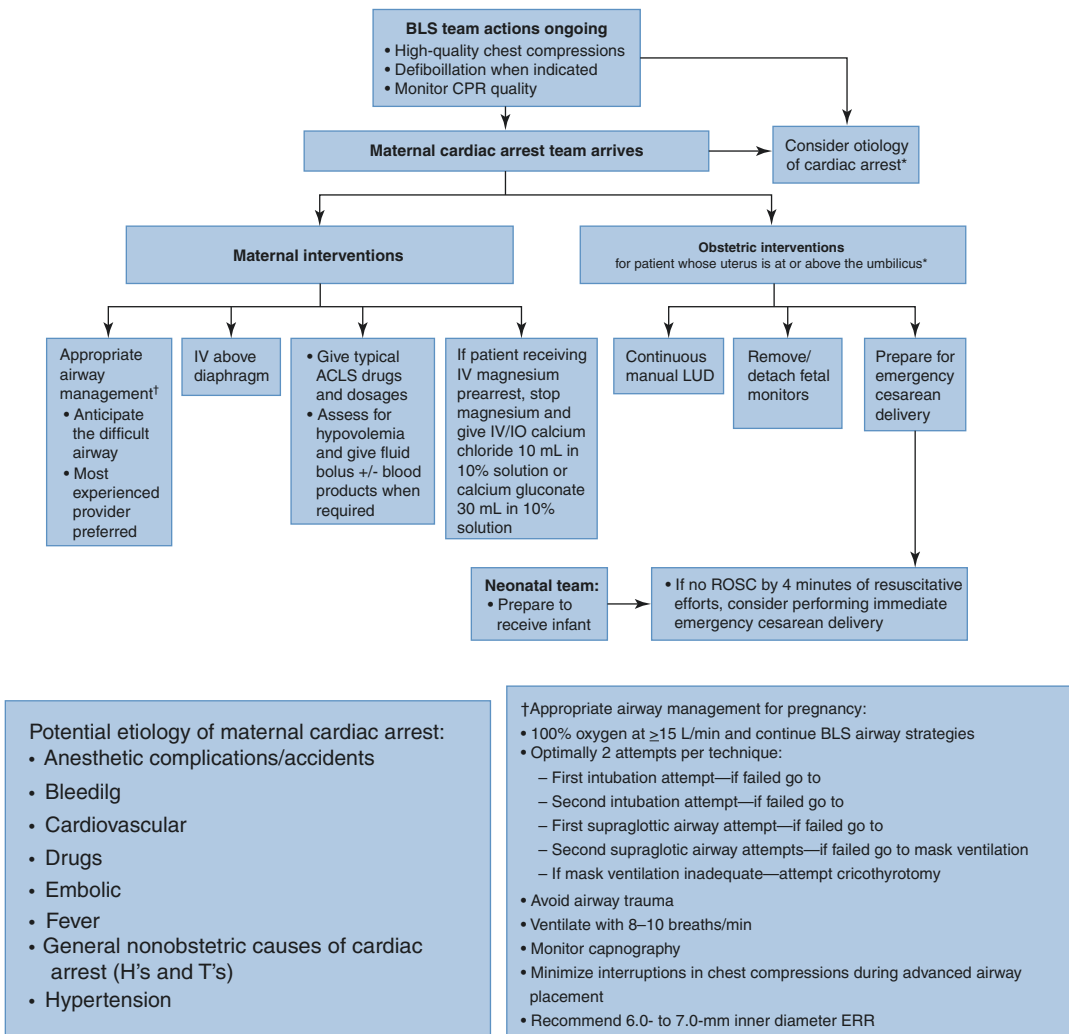
### 2.3.3 Hemorrhage Management

#### 2.3.3.1 Cardiopulmonary Resuscitation

Hypovolemia will manifest as thready pulses, tachycardia, flattened neck veins, pallor, and prolonged capillary refill. The systolic blood pressure is approximately 80 mmHg if a radial pulse

is palpable. The absence of carotid and peripheral pulses indicates pulseless electrical activity, and *Advanced Cardiovascular Life Support* (ACLS) protocols should be initiated. If defibrillation is unnecessary, standard ACLS voltage should be used (Fig. 2.4).

There is no evidence that the current harms the fetus from defibrillation [159]. External fetal monitors should be removed before delivering shocks [159]. Chest compressions should be carried out to understand that the maternal heart is displaced upward in the chest by the gravid uterus at advanced gestations, guiding hand placement [159].



**Fig. 2.4** Maternal cardiac arrest algorithm. (Reproduced with permission from [158])



Cardiopulmonary resuscitation (CPR) should not be interrupted to administer medications because they get circulated with compressions [160]. Administration of medications in pregnancy through lower extremity lines should be avoided because they may not adequately reach the maternal heart because of venous compression by the gravid uterus [160].

Palpable femoral pulses are not reliable indicators of blood flow during CPR because the retrograde flow in the femoral vein could mimic femoral artery pulsations [160]. A carotid pulse during CPR is not an indicator of adequate cerebral or coronary blood flow [160]. An end-tidal CO<sub>2</sub> indicates adequate CPR and the return of spontaneous circulation [160].

### 2.3.3.2 Major Hemorrhage

Major obstetric hemorrhage is a blood loss of  $\geq 2500$  mL, transfusion of 5 units of packed red blood cells (pRBC), or treatment of a coagulopathy [161]. Transfusion of blood and blood products in trauma and major bleeding is changing due to experience in military medicine. Resuscitation in obstetric hemorrhage is similar to that in trauma. Both aim to stop bleeding, maintain efficient oxygen delivery, and prevent the development of the “lethal triad”—acidosis, hypothermia, and coagulopathy. Protocols for defibrillation and doses of medications remain unchanged in pregnancy. Obstetric resuscitation starts with the IV fluids and pRBC, followed by clotting products and platelets, often guided by coagulation studies that delay treatment [162]. The *UK National Patient Safety Agency* recommends monitoring laboratory blood tests during massive transfusions and that administration of blood and blood products should not be delayed while awaiting results [161–163]. Resuscitation of bleeding patients with crystalloid, colloid, and plasma-poor pRBC simultaneously when clotting factors are consumed results in plasma coagulation factors falling to  $<40\%$  and typically occurs before 10 units of pRBC have been given

[164]. Disseminated intravascular coagulopathy in obstetric hemorrhage can also occur early, especially if the bleeding is not treated rapidly. Early treatment of massive hemorrhage after trauma using fresh frozen plasma (FFP) and pRBC in a 1:1 ratio improves survival [164–167]. Military guidelines for hemorrhagic shock also recommend the administration of platelets in a 1:1 ratio with pRBC [165–167].

Prevention of coagulopathy should be better than its treatment and requires anticipation [164]. Some authors advise that clotting factors should be replaced on clinical grounds rather than laboratory results [165, 167]. The *Association of Anesthetists of Great Britain and Ireland* recommends an early infusion of FFP (15 mL/kg) to prevent hemostatic failure. It may need to be started if a senior clinician anticipates massive bleeding [168]. This guideline emphasizes the importance of preventing hemostatic failure because, once established, standard regimens of FFP infusion are likely to be inadequate and larger volumes will be required with greater risk to the patient and cost implications for the hospital [168].

A ratio of 6:4:1 for pRBC/FFP/platelets has been suggested for massive obstetric bleeding. If bleeding continues after initial treatment, consideration should be given to increasing an FFP to a ratio of 4:4:1 [163].

Point-of-care tests can measure hemoglobin concentration and the coagulation profile and guide blood product replacement following initial resuscitation.

Fibrinogen concentrations are also greater in pregnancy; the optimal posttransfusion fibrinogen concentration has been suggested as 1.0–2.0 g/L [162]. The high ratios of pRBC to coagulation products recommended for other types of trauma may not be required in obstetric patients. In contrast, greater replacement of fibrinogen may be necessary. Evidence supports a 1:1:1 ratio of pRBC/FFP/platelets in trauma, but less in obstetrics [162, 165–167].

Maintenance of a platelet count of  $50\text{--}100 \times 10^9/\text{L}$  has been suggested and used as a guide in conjunction with the patient's clinical condition [162]. pRBC/platelet ratios of 5:2 and 5:1 showed good results [162, 169]. Guidelines

suggest that recombinant factor VIIa (rFVIIa) should be considered before hysterectomy if hemostatic failure and hemorrhage continue despite optimal blood product replacement and obstetric management [162, 170]. Arterial thrombosis is a potential complication of rFVIIa use, but has not been reported in a case series of 15 patients [170]. Its safety in the obstetric population is unproven with a significant cost implication. Using thromboelastography and thromboelastometry to guide optimum ratios of blood product replacement during obstetric hemorrhage may be limited by the time during the initial resuscitation phase, and there is limited familiarity with their use in obstetrics [161–163].

Liberal oxygen and fluids administration when the bicarbonate level is low improves tissue perfusion and fetal oxygenation [171, 172].

### 2.3.3.3 Fetal Assessment

Fetal injury can result from major maternal bleeding, direct fetal trauma (see Chap. 5), or both.

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# Increased Intra-abdominal Pressure

# 3

## Abstract

Normal pregnancy leads to chronically increased intra-abdominal pressure (IAP). Pregnancy is a condition where multiple factors such as obesity, preeclampsia, or postpartum hemorrhage may lead to the overdiagnosis of abdominal compartment syndrome (ACS). When raised IAP is detected and treated, ACS may often be avoided, especially with the adoption of newer resuscitation strategies. There is little data regarding physiologic and pathophysiologic IAP in pregnancy. Current consensus guidelines group pregnancy and morbid obesity together as chronically compensated intra-abdominal hypertension (IAH) states. Both operative and nonoperative conditions can cause increased IAP. Despite the limited understanding of IAH in maternal care, even less is known regarding its effects on the fetus. Whether there are subclinical effects of even modest elevations of maternal IAP on the fetus is completely unknown. Therefore, IAP should be measured in all critically ill pregnant patients. Treatment options, including nonoperative and operative strategies, for its normalization should be carried out immediately after verifying increased IAP in pregnancy.

## 3.1 Physiology and Pathophysiology

### 3.1.1 Introduction

In the second and third trimesters of pregnancy, the uterus occupies a major part of the abdominal cavity. Due to hormonal influences during pregnancy, the abdominal wall slowly stretches, increasing its compliance and reducing the potential for increased IAP caused by the expanding uterus. As a result, end-organ dysfunction, as in critically ill patients with acute primary or secondary IAH, is rare because the body has time to adapt to the slowly increasing IAP levels during pregnancy. However, acute IAP increase from any cause (e.g., bleeding or pneumoperitoneum during laparoscopy) compromises uterine and fetal perfusion [1].

Obstetric patients require admission to critical care units at rates ranging from <1% of deliveries in high-income countries to 2–43.6% in low- to middle-income countries [2–4]. The mortality rate of these women ranges from <1% to >40% [3]. The most common causes of intensive care unit admission include hypertensive disorders of pregnancy, bleeding, and infection or sepsis [2, 3]. Each of these is an independent risk factor for intra-abdominal hypertension



(IAH) and abdominal compartment syndrome (ACS) [5, 6]. These illnesses, most commonly preeclampsia and obstetric hemorrhage, can result in significant morbidity and mortality in both mother and newborn [7, 8]. Further complicating the situation, intensivists are often unfamiliar with maternal-fetal physiology in health and critical illness, including the possible impact of increased intra-abdominal pressure (IAP) and IAH on such conditions [7]. Pregnancy is a condition where multiple factors such as obesity, preeclampsia, or postpartum hemorrhage may lead to the overdiagnosis of ACS. Fortunately, the incidence of IAH in critically ill obstetric patients is only 6% [9].

The first seminal work about IAH in pregnancy is from 1913 by an obstetrician Paramore, Hunterian Professor of the Royal College of Surgeons of England [10].

### 3.1.2 The Physiology of Normal Pregnancy

The maternal physiologic changes are multisystemic during pregnancy due to the adaptation to accommodate the gravid uterus. On average, the uterus contributes 1 kg to the overall weight gain in pregnancy, while the amniotic fluid, fetus, and placenta comprise approximately 5 kg in additional weight [11]. To accommodate uterine growth, the thoracic cage increases in both anteroposterior and transverse diameters [11]. The hormone relaxin, released by the corpus luteum and placenta, results in the targeted softening of the ligamentous structures to compensate for uterine growth [12]. The diaphragm becomes elevated due to being pushed cephalad by the uterus, impeding the functional residual capacity by at least 20% [11]. Tidal volume increases and is associated with a 45% increase in a minute and alveolar ventilation [11]. Overall maternal metabolic rate, oxygen consumption ( $\text{VO}_2$ ), gas exchange, and acid/base balance are affected by several factors, including the growth of the fetoplacental unit, progesterone levels, and  $\text{CO}_2$  production.

Maternal  $\text{VO}_2$  increases by 15–20% [13]. The resulting respiratory alkalosis is renally compensated with increased ventilation by reducing serum bicarbonate to 20 mEq/L and total buffer base capacity to 5 mEq/L [11]. Thus, the parturient is more vulnerable to hypoxemia and acidemia when critically ill, with less physiologic reserve than nonpregnant [13]. Also, a 50% increase in plasma volume results in dilutional anemia and an overall rise in circulating blood volume of 40% [11, 13]. Cardiac output increases by 30–50%; blood flow to the gravid uterus increased tenfold [13]. After 20 weeks of gestation, the uterus size can cause a mechanical aortocaval obstruction while fully supine. The ‘supine-hypotensive syndrome’ result is a significant loss of venous return for which the cardiovascular system cannot compensate [11]. However, most women develop collateral circulation through interosseous vertebral, paravertebral, epidural, and ovarian venous systems, less impacted by increased IAP [11]. Those suffering from supine-hypotensive syndrome likely do not develop adequate collateral circulation [14]. While only approximately 8% of women at term experience this life-threatening situation, significant compression of the inferior vena cava while supine occurs in most women [11, 14]. Whether elevated IAP can exacerbate aortocaval compression and has a relationship with this syndrome is unknown. Thus, due to the myriad of hormonal, mechano-physiologic changes, the majority of parturients are well compensated for the exponential growth of their fetus in a relatively short duration of time.

### 3.1.3 Intra-abdominal Pressure in Normal Pregnancy

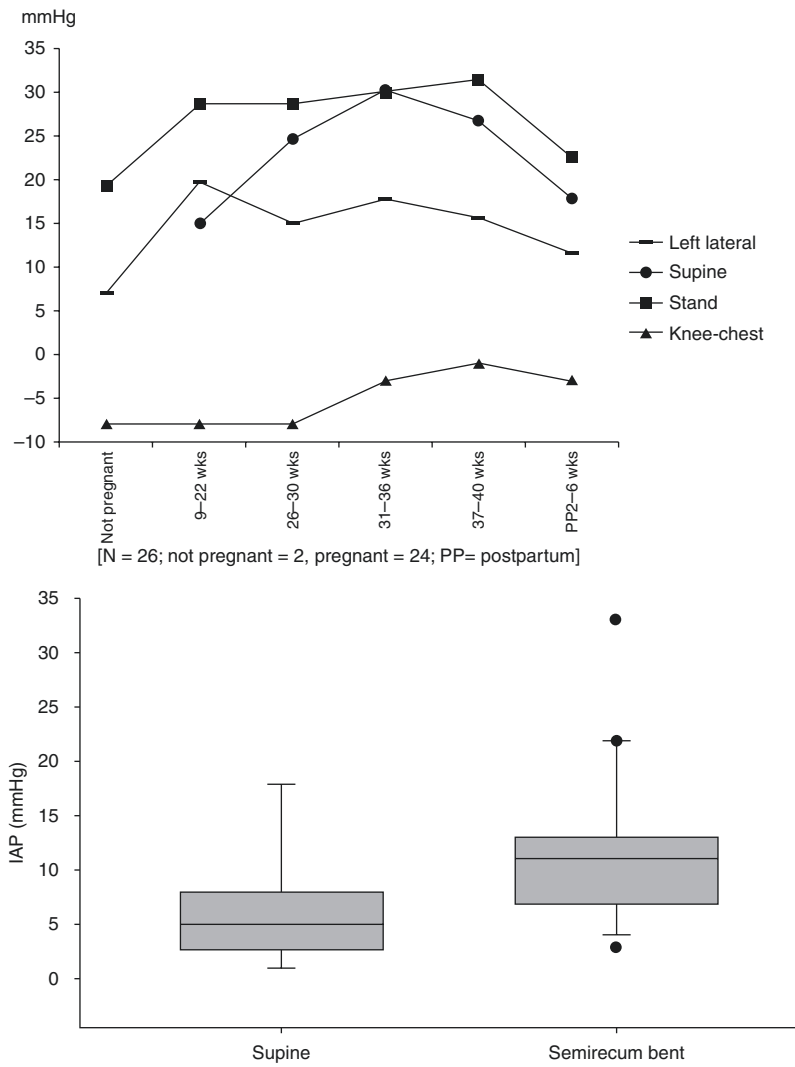
Christian Friedrich Schatz [15] in 1872 and Carl Schroeder [16] in 1886 suggested an adjustment of the abdominal muscles to meet distention by the pregnant uterus. Although with some errors, they claimed that the pressure is 4–5 mmHg lower in the dorsal than in the sitting or standing positions and is negative in the knee-chest or

knee-elbow positions, even  $-2$  to  $-4$  mmHg. During pregnancy, IAP rises slightly though not in proportion to the increase in the size of the uterus, until the last month, when usually the abdominal muscles are stretched beyond their ability to respond, and there is usually a fall of pressure below normal. The R.H. Paramore obtained further evidence through rectal manometry in 1913 [10]. The data were extracted for the standing, supine, left lateral, and knee-chest positions. The highest IAP mean value is in the standing position, and the lowest positive IAP mean value is in the left lateral position. The knee-chest position (inversion of the abdominal orientation)

produced a negative pressure mean value (Fig. 3.1). There is an issue with accurate measurement because the probes inserted in the lower abdomen (rectum, bladder) could produce a higher IAP in the lower than in the upper abdomen. Also, the IAP measured from the second trimester onwards may not be an accurate marker of actual IAP [19]. This is partly due to the compression of the gravid uterus on the bladder, falsely raising the IAP.

Recently, intravesical measurements in healthy term parturients obtained under spinal anesthesia before elective Cesarean section (CS) found the median IAP in a leftward tilted position

**Fig. 3.1** (a) Mean intra-abdominal pressure by position and gestational age transrectally. (Reproduced with permission from [17] under the CC BY-NC-ND 3.0), and (b) 1 h post-Cesarean section intravesically (significantly lower in supine position) [18]



to be  $22 \pm 2.9$  mmHg (range 15–29 mmHg) [20]. These IAP values are actually in the threshold range for ACS if organ failure were also present [21]. However, the methodology could have created some bias, leading to overestimating IAP values. The dermatome level of spinal anesthetic was unknown, leading to possible underrelaxed abdominal wall muscle, and 50 mL instead of 25 mL was instilled in the bladder. After neonatal delivery, the IAP dropped significantly to a median IAP of 16 mmHg (range 11–24 mmHg) [20]. Another issue is the unspecified degree of left lateral tilt during the IAP measurements, making it difficult to reconcile if these measurements reflected the actual IAP or the weight of the gravid uterus on the bladder itself. There is debate about the degree of tilt required to minimize compression of the IVC by the uterus [22, 23]. Under spinal anesthesia, there was significantly higher IAP in the supine position than the left lateral tilt of  $10^\circ$ , with the reference point held constant by placing the bladder pressure transducer in a line adjacent to the patient on an intravenous pole [19]. Compressing the bladder by the gravid uterus falsely elevates the IAP values when fully supine. Also, there is a concern regarding the positioning of ventilated patients fully supine to measure IAP while increasing aspiration risks [24–26]. Sensory block under spinal anesthesia, at least at the level of T6, leads to paralysis of abdominal muscles, altered wall compliance, and changes in IAP. These findings may not be replicable in critically ill patients without a spinal block.

Left lateral tilt has become the standard of care in CS, particularly after spinal anesthesia, to both facilitate CS and alleviate potential aortocaval compression while supine [22]. A tilt of  $15^\circ$  is generally recommended [22].

Proposed normal IAP raises with pregnancy progression. Obstetrics-specific IAP values for diagnosing IAH and ACS are presented in Table 3.1. These values are based partly on nor-

**Table 3.1** The IAP in healthy pregnancy [27]

| Gestational age | Mean IAP (mmHg) |
|-----------------|-----------------|
| <20 weeks       | 5–7             |
| 20–26 week      | 8–10            |
| 27–32 week      | 11–12           |
| >32 weeks       | 13–14           |
| Postpartum      | 8–10            |

*IAP* intra-abdominal pressure

mal abdominal compliance and the volume of the fetus. IAH in pregnancy is a sustained or repeated pathological elevation in  $\text{IAP} \geq 14$  mmHg. ACS in pregnancy is a sustained  $\text{IAP} > 25$  mmHg associated with new organ failure/dysfunction. Women with preeclampsia have a slightly higher IAP than healthy pregnant women and may have signs/symptoms of end-organ failure. Postpartum patients with IAH may have the severity graded using the same scale as nonpregnant adults (Table 3.2).

Guidelines group pregnancy and morbid obesity as chronically compensated states of IAH [28]. Unlike pregnancy, chronic obesity is the deposition of fat diffusely throughout the abdominal cavity and does not last a fixed period. This anatomical difference could be significant, given that the standard of measurement of IAP uses the intravesical pressure as a surrogate, the location of which rests in the pelvis.

### 3.1.4 Pathophysiology of IAH/ACS

#### 3.1.4.1 Physical Laws of IAP in Pregnancy

The relationship between IAP and pregnancy is defined by the equation  $\text{DIAP} = \text{DIAV}/\text{Cab}$  (change in IAP = change in intra-abdominal volume/abdominal compliance) [29]. This equation considers the magnitude or volume of the abdomen in the supine position, which is appropriate for critically ill patients [29]. Abdominal compliance or elasticity is a volume change divided by a change in pressure (L/mmHg) and describes tolerance to increases in intra-abdominal volume [29]. However, pregnant women are mobile, and IAP in pregnancy varies with position [10, 18–20, 30]. Therefore, the equation is expanded to incorporate



**Table 3.2** Definitions and diagnostic criteria for IAP, IAH, and ACS

| Definition                                                                                                                                             | Diagnostic criteria                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>IAP</b> is the steady-state pressure concealed within the abdominal cavity                                                                          | The reference standard for intermittent IAP measurements is via the bladder with a maximal instillation volume of 25 mL of sterile saline<br>IAP should be expressed in mmHg and measured at end-expiration in the supine position after ensuring that abdominal muscle contractions are absent and with the transducer zeroed at the level of the midaxillary line                                                                                                            |
| IAP is approximately 5–7 mmHg in critically ill adults                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>IAH</b> is a sustained or repeated pathological elevation in IAP $\geq 12$ mmHg                                                                     | <b>Grade I</b> , IAP 12–15 mmHg<br><b>Grade II</b> , IAP 16–20 mmHg<br><b>Grade III</b> , IAP 21–25 mmHg<br><b>Grade IV</b> , IAP $>25$ mmHg                                                                                                                                                                                                                                                                                                                                   |
| <b>ACS</b> is a sustained IAP $>20$ mmHg (with or without an APP $<60$ mmHg) that is associated with new organ dysfunction/failure                     | <b>Primary IAH or ACS</b> is a condition associated with injury or disease in the abdominopelvic region that frequently requires early surgical or interventional radiological intervention<br><b>Secondary IAH or ACS</b> refers to conditions that do not originate from the abdominopelvic region<br><b>Recurrent IAH or ACS</b> refers to the condition in which IAH or ACS redevelops following previous surgical or medical treatment of primary or secondary IAH or ACS |
| APP = MAP – IAP                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| A <b>polycompartment syndrome</b> is a condition where two or more anatomical compartments have elevated compartmental pressures                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Abdominal compliance</b> is a measure of the ease of abdominal expansion, which is determined by the elasticity of the abdominal wall and diaphragm | It should be expressed as the change in intra-abdominal volume per change in IAP                                                                                                                                                                                                                                                                                                                                                                                               |
| The <b>open abdomen</b> requires a temporary abdominal closure due to the skin and fascia not being closed after laparotomy                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

Reproduced with permission from [28]

ACS abdominal compartment syndrome, APP abdominal perfusion pressure, IAH intra-abdominal hypertension, IAP intra-abdominal pressure, MAP mean arterial pressure

the unique vector dynamics of the maternal abdomen, as vector force more accurately describes both volume magnitude and force direction (consideration of weight due to gravity):  $VF = VM + D$  (vector force = volume magnitude + direction) [29, 31]. Hence, applied to pregnancy, the formula is  $DIAP-P = DIAVF/Cab$  (change in IAP in pregnancy = change in abdominal vector force (volume + direction)/abdominal compliance).

The formula  $DIAP = DIAV/Cab$  assumes a curvilinear relationship between abdominal volume and pressure dependent on abdominal wall compliance [29]. Following the initial linear slope, an exponential increase in pressure occurs once the critical volume is attained. This formula and curvilinear relationship reflect the principle of Laplace's Law, which addresses the relation-

ship between radius (volume), pressure, and wall tension [31]. The greater the radius (volume), the greater wall tension is required to withstand internal fluid pressure. Based on these principles and at constant atmospheric pressure, the formula  $DIAP-P = DIAVF/Cab$  assumes a similar curvilinear relationship between abdominal vector force and IAP-P, dependent on abdominal wall compliance.

IAP in women during the latter stages of pregnancy increases into the range of IAH, perhaps leading to a reduced "buffer" for the pressure to increase before ACS for any underlying cause of IAP. Mulier found a linear relationship between IAP and volume to calculate the abdominal wall elastance [32] and even decreased significantly with increased age and gravidity [33].

The IAP in nonpregnant, healthy adults ranges from 0 to 7 mmHg and increases to 10–11 mmHg in critically ill, non-obstetric patients [34]. A sustained IAP increase of  $\geq 12$  mmHg represents IAH (Table 3.2); IAP  $> 20$  mmHg associated with new-onset organ dysfunction represents ACS [28]. *Abdominal perfusion pressure* is estimated by subtracting IAP from mean arterial pressure, and values  $> 55$  to 60 mmHg suggest adequate abdominal organ perfusion better than relying on mean arterial pressure or IAP alone. However, current recommendations do not support using abdominal perfusion pressure to guide resuscitation and fluid management for ACS [28].

#### 3.1.4.2 Digestive System Pathophysiology

IAH/ACS results in hemodynamic shifts, including decreased venous, arterial, and microcirculatory flow and increased systemic resistance resulting in ischemia-reperfusion injury [29]. This compromised microcirculatory flow and oxidative stress cause epithelial damage and disruption of the mucosal integrity in the intestinal epithelium, leading to intestinal permeability [35, 36]. Epithelial integrity is further compromised by losing intercellular tight junction integrity and loss of intestinal barrier function [37]. This leads to the translocation of LPS endotoxin from Gram-negative bacteria to the mesenteric lymph nodes, the portal vein, and the liver [35, 36]. The exposure of Kupffer cells to LPS endotoxin initiates a cytotoxic immune response. Multiple proinflammatory cytokines mediate the endotoxic effects of LPS in the systemic circulation. This results in a systemic inflammatory response, oxidative stress, and subsequent multi-organ failure [38, 39]. The LPS response is mediated by the liver, while the placenta mediates the immune response characteristic of preeclampsia.

In addition to intestinal ischemia-reperfusion injury resulting in mucosal epithelial injury, the loss of barrier function may be caused by two environmental factors: abnormal exposure to enteric and pathogenic bacteria and small intestine exposure to dietary gliadin [40, 41]. Therefore, intestinal permeability is caused by (1) intestinal ischemia-reperfusion injury, (2)

exposure to enteric pathogenic bacteria, and (3) dietary gliadin.

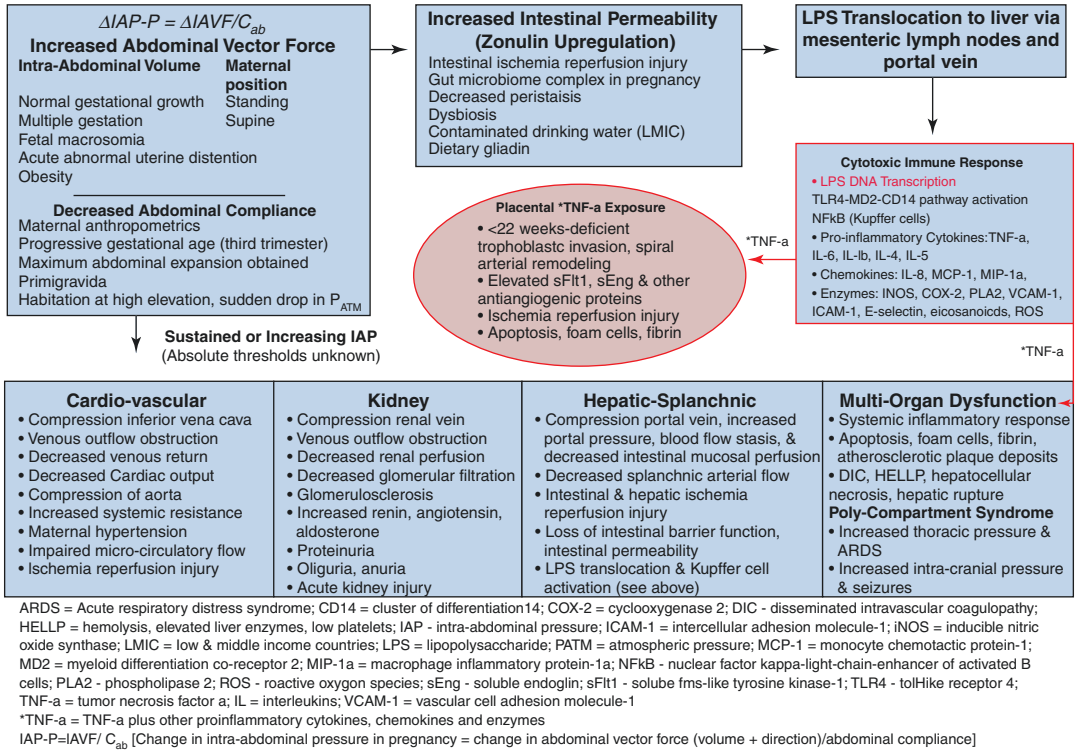
#### 3.1.4.3 IAH/ACS and the Fetus

Despite the limited understanding of maternal IAH, even less is known regarding its effects on the fetus. IAH decreases uterine blood flow and induces compensatory fetal hypertension [42], such as during laparoscopy, even with inert gases rather than CO<sub>2</sub>. In a gravid rabbit model, intra-amniotic pressure (IAMNP) was linearly related to IAP ( $\text{IAMNP} = \text{IAP} \times 0.8 + 2.0$ ). Further, the elevation of IAMNP to 15.6 cmH<sub>2</sub>O via the elevation of the IAP (to 17 cmH<sub>2</sub>O) altered the contractile properties of the fetal bladder [43]. One hypothesis regarding the fetal-placental unit is that elevated IAMNP is translated to elevated fetal IAP, both influenced by the elevations of maternal IAP [44]. Through this mechanism, elevated fetal IAP could result in increased urethral resistance, the chronicity of which could lead to abnormal development of the bladder detrusor muscles, resultant dysfunctional voiding in children, and possibly urinary tract anomalies [44].

In addition to increased IAP, pregnant rats exposed to LPS had higher serum TNF- $\alpha$  levels. TNF- $\alpha$  mediated inflammation resulted in [45, 46]: (1) deficient trophoblastic invasion and spiral artery remodeling, (2) altered uteroplacental hemodynamics and increased average spiral artery resistance index, (3) placental nitrosative stress, (4) increased maternal mean arterial pressure, (5) maternal renal structural alterations, including mesangial hypercellularity, occlusion of capillary loops; and (6) significant maternal elevation of protein:creatinine ratios and proteinuria, (7) fetal death in a dose-dependent manner within 3–4 h of LPS exposure, (8) fetal growth restriction in the surviving fetuses, and (9) maternal coagulopathy in cases of fetal death.

## 3.2 Etiopathogenesis

IAH/ACS in pregnancy presumes a causal pathway, which may be intrinsically or environmentally triggered (Fig. 3.2). This hypothesis includes



**Fig. 3.2** Intra-abdominal hypertension in pregnancy etiology pathway. (Reproduced with permission from [17] under the CC BY-NC-ND 3.0)

the relationship between independent and dependent variables, the temporal-spatial positioning of etiological factors, and the role of genetic factors.

**3.2.1 Nonoperative Conditions**

**3.2.1.1 Preeclampsia**

François Mauriceau (Fig. 3.3) noted the preponderance of ‘toxemia’ of pregnancy in primiparas in 1694 and described some preeclampsia clinical manifestations [48]. In the 1900s, Paramore suggested uncompensated elevated IAP as a possible etiologic factor in the development of preeclampsia [10, 49]. He also hypothesized that nulliparous and muscular women were prone to spastic abdominal wall tone resulting in elevated IAP, compromising perfusion pressure to the abdominopelvic viscera [10, 49].

Preeclampsia is part of a spectrum of hypertensive disorders of pregnancy, defined as the presence of arterial hypertension (blood pressure BP  $\geq 140/90$  mmHg) on 2 occasions, at least 6 h apart, but without evidence of end-organ damage, of a woman who was normotensive before 20 weeks’ gestation and proteinuria ( $>0.3$  g/24 h). With pre-existing essential hypertension, preeclampsia is diagnosed if systolic BP has increased by 30 mmHg or if diastolic BP has increased by 15 mmHg [50]. Patients with preeclampsia have low colloid osmotic pressure with significant third spacing resulting in elevated IAP. When sustained or increasing, IAP in pregnancy  $\geq 12$  mmHg leads to hemodynamic shifts, intestinal ischemia-reperfusion injury, translocation of LPS endotoxin to the liver, systemic cytotoxic immune response, multi-organ dysfunction, and poly-compartment syndrome [17]. The pathophysiology of preeclampsia is shown in Fig. 3.4.

Clinical symptoms and organ failure that can be seen in patients with preeclampsia are similar to those of patients with IAH.



**Fig. 3.3** François Mauriceau (Paris 1637–Paris 1709) received his training in obstetrics at the Hôtel-Dieu. He was a leading obstetrician in seventeenth-century Europe. In 1668, he published *Traité des Maladies des Femmes Grosses et Accouchées*, a book that helped establish obstetrics as a science. (Reproduced with permission from [47] under CC PD-Art tag)

The antepartum (18.3 cmH<sub>2</sub>O vs. 13.3 cmH<sub>2</sub>O) and postpartum IAP levels were significantly higher in preeclampsia than in healthy pregnant patients [52]. Abdominal hypertension was identified in >80% of preeclamptic patients. Those with severe preeclampsia with oliguria had the highest IAP level [52].

These clinical manifestations have been well described as early as the mid-1600s [48]. The most common hypothesis is that abnormal placentation occurs during the myometrial trophoblastic invasion in the second trimester [50], leading to placental ischemia and the release of

angiogenic toxins, causing widespread endothelial dysfunction [53] and generalized inflammation. The worldwide incidence in pregnancy is 3–5% [50].

The endothelial dysfunction leads to increased vascular permeability and possible hypoalbuminemia, which cause the third spacing of fluids resulting in significant intra-abdominal fluid collections. The fluid extravasation causes relative intravascular depletion, which may cause decreased urine output. Immediate postpartum IAPs are higher than those in the normal postoperative population [18] and more prominent in pregnancies complicated with arterial hypertensive disorders of pregnancy/HELLP syndrome. The combination of higher IAPs and abnormal renal function may falsely lead the physician to diagnose ACS. This may, in turn, lead to unnecessarily aggressive management options. Therefore, preeclampsia should be ruled out when IAP/IAH accompanies proteinuria after the 20th week of gestation.

### 3.2.1.2 HELLP Syndrome

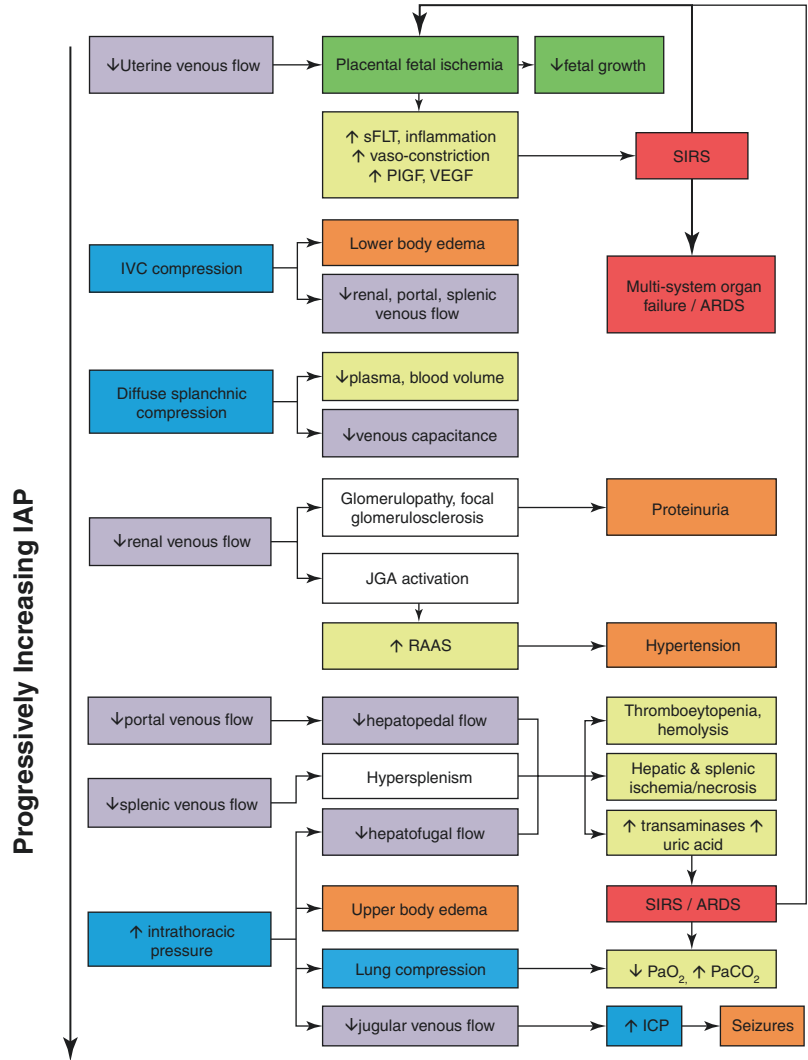
HELLP is considered a severe variant of preeclampsia and manifests as a syndrome of hemolysis, elevated liver enzymes, and low platelet count [53]. Due to hormonal influences during pregnancy, the abdominal wall is slowly stretched, increasing its compliance and reducing the potential for increased IAP caused by the expanding uterus. Spontaneous rupture of a hepatic subcapsular hematoma (see Sect. 26.1) is a complication of HELLP syndrome and results in intra-abdominal hemorrhage. Continued intraperitoneal hemorrhage and fluid resuscitation can lead to IAH and ACS, along with hemorrhagic shock [54].

### 3.2.1.3 Ovarian Hyperstimulation Syndrome

Ovarian hyperstimulation syndrome (OHSS) is an uncommon but increasingly common complication of ovulation induction for assisted reproduction [55, 56]. Other risk factors are presented in Table 3.3.

The mechanism is thought to be mediated by vasoactive cytokines in response to exogenous

**Fig. 3.4** Presumed pathophysiology of preeclampsia/eclampsia (purple—direct effects on venous flow; blue—increased pressures; green—direct effects on the fetus; orange—clinical signs; yellow—end effects of increased IAP; red—life-threatening systemic outcomes). *IAP* intra-abdominal pressure, *sFLT* placental soluble fms-like tyrosine kinase 1, *PIGF* placental growth factor, *VEGF* vasoactive endothelial growth factor, *SIRS* septic inflammatory response syndrome, *ARDS* adult respiratory distress syndrome, *IVC* inferior vena cava, *JGA* juxta-glomerular apparatus, *ACE* angiotensin-converting enzyme, *ICP* intracranial pressure [51]



**Table. 3.3** Risk factors associated with the development of ovarian hyperstimulation syndrome

|                                                                    |
|--------------------------------------------------------------------|
| Young age (<35 years)                                              |
| Low body mass index—asthenic habitus                               |
| Polycystic ovarian syndrome                                        |
| History of atopy or allergies                                      |
| Previous episode of OHSS                                           |
| Pregnancy                                                          |
| Higher or repeated doses of exogenous human chorionic gonadotropin |
| Gonadotropin-releasing hormone—agonist protocol                    |
| Use of Clomiphene citrate                                          |
| Increased number of developing follicles (>35)                     |
| ≥14 oocytes retrieved                                              |
| Elevated serum estradiol (>2500 pg/mL)                             |

Reproduced with permission from [57]

human chorionic gonadotropin administration [58]. Vascular endothelial growth factor increases vascular permeability by reducing the colloid osmotic gradient favoring leakage to the extra-vascular space [55, 59]. This “third spacing” leads to intravascular volume depletion, resulting in hypotension. In its most severe form, massive and rapid accumulation of abdominal ascites results in an overt ACS [58]. Because hypotension leads to decreased venous pressure and reduced venous return, a decreased cardiac output might be expected; however, studies have found the cardiac output increased in OHSS while mean arterial pressure and peripheral vas-



cular resistance decreased [60]. These findings implied the accompanying arterial vasodilation in OHSS [61]. Hypotension affects organ function. Reduced kidney perfusion leads to a reduced glomerular filtration rate and can result in oliguria (Fig. 3.5). Transvaginal oocyte retrieval can inoculate infection to ascitic fluid [62]. The compliance of the abdominal wall gradually increases in patients with OHSS with larger ascites volumes needed to result in the same drop in IAP [6]. The compliance can be calculated by the change in intra-abdominal volume divided by the change in IAP (see Sect. 3.1.4.1).

#### 3.2.1.4 Obesity

Obesity causes chronically elevated IAP (7–14 mmHg) [6], and prepregnancy body mass

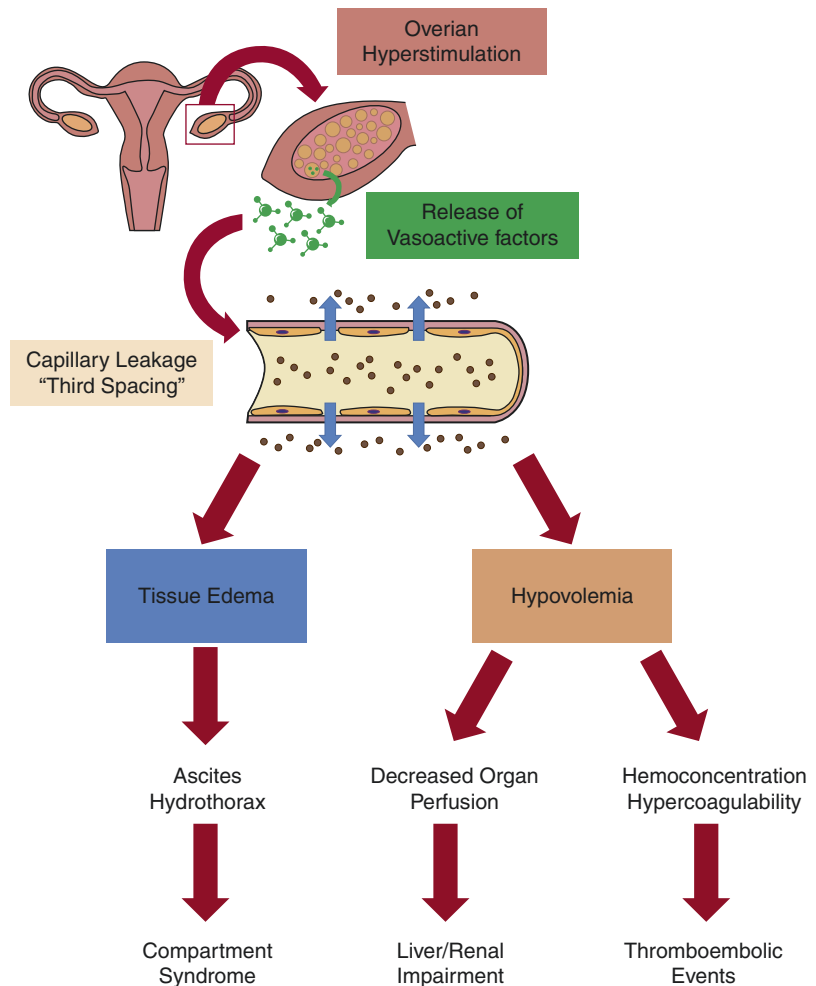
index (BMI) significantly correlates to elevated post-CS IAP [18]. However, no evidence exists that the effects of pregnancy and obesity on IAP are additive [27].

#### 3.2.1.5 Obstetric/Gynecologic Conditions

A pathological increase in intra-abdominal volume is seen with multiple gestations, fetal macrosomia, polyhydramnios, fetal/placental hydrops, and large hydatidiform moles [63, 64].

Like OHSS, rapid growth in abdominal girth, dyspnea, abdominal pain, and other overt symptoms of ACS in other gynecological conditions must also be considered in the differentials. Patients undergoing ovulation induction are also at increased risk of ovarian torsion and ectopic

**Fig. 3.5** Pathophysiology of ovarian hyperstimulation syndrome. (Reproduced with permission from [57])



pregnancy [56]. Meigs' syndrome, solid ovarian tumors associated with hydrothorax and ascites, has been described similarly to OHSS in presenting with symptoms of ACS [65].

### 3.2.2 Operative Conditions

Normal postoperative pressures following abdominal surgery range from 3 to 15 mmHg in the general population [66]. There is a lack of information about IAP in an entirely female and obstetric population.

#### 3.2.2.1 Laparoscopic Pneumoperitoneum

Laparoscopy during pregnancy potentially exposes the fetus to risks from (1) trocar placement, (2) the effects of CO<sub>2</sub> on the developing fetus and the long-term effects of this exposure with the significant fetal loss, and (3) consequences of the increased intra-abdominal pressure on the fetus (See Chap. 4).

Several intraperitoneal access techniques for delivering pneumoperitoneum exist. One is using an open (*Hasson*) technique under direct vision. Another is a Veress needle inserted 2–4 cm above the uterus on the left or the RUQ in the midclavicular line approximately 1–2 cm below the costal margin (*Palmer's point*). Veress needle can be inserted under the guidance of the US. Some claim a higher risk of perforation of intra-abdominal organs or pneumoamnion, especially in advanced pregnancy [67, 68]. An optical trocar (under direct vision) can be used for entering the abdomen after pneumoperitoneum created by the Veress needle, as in bariatric surgery. Optical trocars can be used even without pneumoperitoneum.

The use of elective laparoscopy in the first trimester of pregnancy is controversial [69] because of the unknown effects of the CO<sub>2</sub> pneumoperitoneum on the developing fetus [70, 71].

There is no increased risk for obstetric outcomes with elective laparoscopy [72, 73]. At the same time, the greater fetal loss in emergency surgery is attributed to intra-peritoneal inflammation or bleeding without changes in obstetric outcomes between the open and laparoscopic approaches [74].

As a general principle, when the fetal-maternal unit is stressed, the mother is “conserved” at the expense of the fetus. For example, during pregnancy, the normally decreased maternal PaCO<sub>2</sub> may ensure adequate transplacental CO<sub>2</sub> diffusion from the fetus to the mother for subsequent pulmonary excretion. CO<sub>2</sub> pneumoperitoneum may cause maternal and subsequent fetal hypercarbia due to the mother's decreased maternal ventilation and increased transperitoneal CO<sub>2</sub> absorption. Experiments on pregnant sheep with CO<sub>2</sub> pneumoperitoneum of 15 mmHg showed a drop in pH into the acidemic range both in the mother and the fetus [70]. After 30 min, a steady state is reached. Hyperventilating the mother brings the pH of both back to normal ranges. There were no changes in PaO<sub>2</sub>. Fetal hemodynamic effects included increased mean heart rate and a mean arterial pressure. After deflation, pH, heart rate, and BP turned to normal. Under the same conditions, nitrous oxide as insufflating gas showed no effects on fetal blood-gas values, heart rate, and BP. This indicates that fetal tachycardia and hypertension are caused by hypercarbia, not increased IAP. The conclusion was that the pneumoperitoneum is not a significant risk to a healthy fetus. It induces progressive, albeit reversible, fetal hypercarbia, acidosis, and tachycardia when pneumoperitoneum pressures exceed 15 mmHg. These effects were minimized using low pneumoperitoneum pressures or nitrous oxide as the insufflation gas [70]. The potentially deleterious effects of short-term fetal hypercarbia are

unknown. However, in high-risk mothers prone to hypercarbia (e.g., chronic lung disease, massive obesity), precautions to decrease maternal hypercarbia by using low-pressure pneumoperitoneum ( $\leq 12$  mmHg) or nitrous oxide as the insufflation gas might be considered. Nitrous oxide has been safely employed during gynecologic laparoscopy.

Others confirmed that an IAP  $\leq 15$  mmHg has no risks. The intrauterine pressure during uterine contractions and coughing (representing intermittent and short periods) is higher [75–77].

Nitrous oxide requires the presence of either hydrogen gas or methane (such as from colonic origin) to be combustible during electrosurgical procedures [70].

The introduction of gas into the peritoneum (closed cavity) has two immediate effects: (1) an increase in IAP and (2) gaseous exchange leading to equilibrium with gases in the blood [78]. Increased IAP can decrease cardiac output by several mechanisms, including direct alteration of venous resistance in the inferior vena cava, total peripheral resistance, and mean systemic pressure [78]. Impaired venous return via compression of the inferior vena cava is of particular concern in the second half of pregnancy since the enlarged uterus can also limit venous return. The uterine compression of the vena cava can be minimized by lateral tilt (see Sect. 3.1.3). The  $\text{CO}_2$  absorbed across the peritoneal surface first equilibrates within the bloodstream with a longer operative time with the skeletal muscle, viscera, and finally, bone. Patients undergoing a prolonged laparoscopy are at risk of maintaining hypercarbia and acidosis postoperatively until all excess  $\text{CO}_2$  is eliminated from the tissue. Hypercarbia and respiratory acidosis can be monitored to some extent by capnography, which measures end-tidal  $\text{CO}_2$  concentration in the endotracheal tubes. If a rise in end-tidal  $\text{CO}_2$  is detected,  $\text{CO}_2$  elimination via the alveoli can be increased using controlled hyperventilation. The limitation of capnography is that while it is sensitive, end-tidal  $\text{CO}_2$  is not foolproof in estimating  $\text{CO}_2$  arterial pressure. When a ventilation-perfusion mismatch is present, and the ventilation is greater relative to perfusion, gas from such

ventilation will contain less  $\text{pCO}_2$  than the actual  $\text{PaCO}_2$ , resulting in falsely normal or low end-tidal  $\text{CO}_2$  readings [79]. A similar discrepancy between end-tidal  $\text{CO}_2$  and  $\text{PaCO}_2$  and subsequent acidosis has been demonstrated in laparoscopy patients with compromised cardiopulmonary status [80]. Monitoring arterial  $\text{PaCO}_2$  and pH is preferable to limit the risk of hypercarbia and acidosis for such patients. The close monitoring of  $\text{CO}_2$  is also important, considering the potential direct effect of  $\text{CO}_2$  in increasing the mean arterial pressure and total peripheral resistance index, leading to increased afterload and limiting cardiac output [81].

Limited studies of pneumoperitoneum in pregnant sheep have demonstrated increased fetal arterial BP, tachycardia, and respiratory acidosis, only partially corrected with alteration in ventilator settings based on maternal capnography results [70, 82]. Intraperitoneal  $\text{CO}_2$  pressures of  $\leq 12$  mmHg are recommended to prevent fetal acidosis [83].  $\text{CO}_2$  pneumoperitoneum created a minimal impact on the patient and the fetus when IAP  $\leq 15$  mmHg is used [70, 84]. Some authors use a pneumoperitoneum of 10 mmHg—low enough to be in the safe range and high enough to gain adequate visualization for a safe procedure [85, 86].

Questions arise regarding the risk of decreased uterine blood flow due to increased IAP from insufflation and the possibility of fetal  $\text{CO}_2$  absorption.  $\text{CO}_2$  used to create pneumoperitoneum could lead to fetal  $\text{CO}_2$  absorption with potential subsequent fetal acidosis. This could be minimized with IAP maintenance  $< 12$  mmHg and minimizing operative time. Clinical and experimental studies found no substantial adverse effects on the fetus when the maximal pneumoperitoneum pressure was limited to 10–12 mmHg, and the operation was less than 60 min [84, 87]. Sheep fetus has sufficient placental flow reserves or compensatory responses to maintain adequate gas exchange during a 1 h, 20 mmHg pneumoperitoneum [88]. Others stress the importance of absorbing carbon monoxide through the peritoneum, produced using monopolar energy. The absorbed carbon monoxide can produce carboxy-hemoglobin and methemoglobin that compete



with hemoglobin in the uptake and transport of oxygen. It is recommended to continually remove the smoke produced by tissue fulguration without an increase in carboxyhemoglobin levels [89, 90]. Harmonic scissors produce vapor-free gas, avoiding the potential effects of carbon monoxide [91]. Another negative effect of electrocautery is the potential for uterine irritation. The CO<sub>2</sub> insufflation into the amniotic cavity of anesthetized ewes produced severe fetal hypercapnia, despite normal maternal CO<sub>2</sub> pressure and pH [92]. However, the possible adverse effect of CO<sub>2</sub> pneumoamnion is most relevant to the future use of fetal surgery and should not be extrapolated to intraperitoneal surgery.

A cardiac output decrease may put the placental and fetal blood flow at risk. However, the effect of increased IAP on venous return is volume-dependent [93]. In relatively hypovolemic subjects, increased IAP decreases venous return. This effect results from elevated venous resistance greater than the concomitant increase in mean systemic pressure. Conversely, in relatively hypervolemic subjects, increased IAP causes minimal compression of the inferior vena cava, and increased mean systemic pressure “pumps” the blood into the inferior vena cava. This effect causes increased venous return and cardiac output resulting from the Starling mechanisms [93]. Therefore, pregnant women are usually hypervolemic because pregnancy is associated with increased circulating blood volume. The pneumoperitoneum should not lead to lower cardiac output or decreased fetal flow. Moreover, moderately increased IAP as in laparoscopy (12–15 mmHg) increases preload at the beginning of pneumoperitoneum as a result of “milking” pooled blood from the splanchnic veins to the systemic circulation and forcing blood to the intravascular compartment from the compressed liver and spleen [94–96].

The anesthesiologist easily corrects maternal respiratory acidosis, but the end-tidal CO<sub>2</sub> may not reflect the fetus’s true pCO<sub>2</sub> and acid-base balance. Alterations in ventilator settings based on maternal end-tidal CO<sub>2</sub> resulted in late and incomplete correction of respiratory acidosis. Therefore, arterial blood gases should be fol-

lowed for accurate monitoring, especially because the end-tidal CO<sub>2</sub> significantly underestimates maternal pCO<sub>2</sub> by 15 mmHg and lags behind it [70]. Fetal hypercarbia, acidosis, possibly tachycardia, and increased fetal arterial pressure are produced by a CO<sub>2</sub> pneumoperitoneum [70]. Again, adverse long-term effects of these physiologic alterations on the fetus are not found but should be avoided, if possible, by close monitoring of maternal indices.

An N<sub>2</sub>O pneumoperitoneum showed none of the ‘acidotic’ changes of CO<sub>2</sub> pneumoperitoneum, but it has not been used due to combustion concerns [70].

### The Postpartum Period

The postpartum patient can eliminate concerns about the fetus. However, several unique characteristics apply to this group. The enlarged uterus is a potential technical factor in the early postpartum period. After CS, the challenges of a recent surgical incision must be considered.

Any conservative treatment course is hampered by these patients’ strong desire to minimize the number of hospital days, recurrent symptoms, and disability. Physiologically, postpartum patients are still recovering from pregnancy and childbirth. Also, separation from a newborn, combined with varying degrees of labile emotions related to the postpartum state, accentuates the usual psychological stresses of illness. If early laparoscopy can be applied to this group, the benefits will be even greater than that reported for the general population.

The enlarged uterus does not hamper exposure, even in the first week. At the time of surgery, the uterine fundus is below the umbilicus. This is consistent with technical success and good exposure in pregnant patients undergoing laparoscopy during the first and second trimesters [97].

The final unique consideration in the postpartum patient is the presence of a healing abdominal incision after CS. Adhesions are rarely encountered after CS. It seems prudent to utilize the minimal IAP of 10 mmHg in CS patients. This may prevent undue mechanical strain on the healing wound, which is necessary for adequate

exposure in these patients. Although evidence suggests a fascial separation, if present, occurs early, it remains to be seen what long-term status these incisions will achieve. The course of the procedure and recovery is identical to the remainder of the patients. No hernia has developed in these patients with a follow-up of 5.5 years [98].

### Combined or Consecutive Operations During the Same Pregnancy

Different emergent procedures are performed during the same pregnancy. Maternal and fetal outcomes depend mostly on the severity of the underlying disease, not the operation and anesthesia. Both open and laparoscopic approaches are allowed. The cholecystectomy is performed first because it looks safer to conduct a cholecystectomy in a stable patient before any significant bleeding potentially encountered with childbirth [99] unless preoperative fetal distress is confirmed.

When a laparoscopic approach is performed with CS, CS should be performed first due to the remote intra-abdominal disease. There are several benefits of such management. First, the fetus has shorter exposure to the consequences of an underlying maternal disease. Second, there is more intra-abdominal space after CS, and the pneumoperitoneum can be increased to 15 mmHg. Third, if the operation cannot be completed by laparoscopy, a separate incision or extension of median laparotomy enables combined procedures.

### Gasless Laparoscopy

To overcome the potential adverse effects of pneumoperitoneum to the fetus, gasless laparoscopic surgery (GLS) was developed during the 1990s [100, 101]. GLS in pregnancy has comparable outcomes to conventional CO<sub>2</sub> laparoscopy, but it is associated with some advantages. Hypercarbia and increased intraperitoneal pressure due to CO<sub>2</sub> insufflation are avoided. Operations can be performed in epidural anesthesia [102].

There are two basic lift systems. The *subcutaneous lift system* [100, 102] has advantages over the *full-thickness wall lift* [101]. First, the surgeon can avoid injury to the gravid uterus, thus reducing the risk of abortion. Second, the subcutaneous lift system can be applied to all patients,

regardless of previous abdominal surgery or unexpected adhesions. Another positive feature of the subcutaneous lift system is eliminating trauma to the peritoneum, which could cause pain and result in adhesions.

Experience with gasless laparoscopy is limited to only 45 patients operated in pregnancy [103–105]. More than 30 cases of non-emergent GLS adnexal mass operations were performed during pregnancy [102, 106–108]. Only six cases of GLS cholecystectomy during pregnancy were published [103, 109]. There is a case of GLS for uterine myomectomy [110]. Three case reports of GLS-treated adnexal torsion during pregnancy were published. Two were successfully performed using the Laparofan (Origin, Menlo Park, CA) [111, 112] and one with Mizuho Co [105].

Gasless laparoscopy is not widely accepted in pregnant populations.

### 3.2.2.2 Burst Abdomen

#### Definition

A *burst abdomen* represents the partial or complete separation of an abdominal wall wound with protrusion or evisceration of abdominal contents. It should be distinguished from wound dehiscence. *Wound dehiscence* and *incisional hernia* are parts of the same wound failure process; timing and the healing of the overlying skin distinguish the two. Wound dehiscence occurs before cutaneous healing, while incisional hernias (see Sect. 19.4) lie under a well-healed skin incision. Evisceration can occur after skin ischemia and subsequent skin dehiscence overlying hernia due to increased IAP. This condition is mostly seen with the (incarcerated) uterus in the giant umbilical hernia (see Sect. 19.2).

#### Incidence and Etiopathogenesis

Burst abdomen during pregnancy develops after incisional hernias (Fig. 3.6) [113, 114], umbilical hernias (Fig. 19.21) [115, 116], and surgical site infections after laparotomy [117–119]. Intra-abdominal sepsis in pregnancy is rare, and

abdominal wall dehiscence following intra-abdominal sepsis is even rarer. Respiratory insufficiency, compensated by the additional use of abdominal respiratory muscles, can cause wound dehiscence [120]. The risk is higher if the underlying disease is causing respiratory insufficiency. For example, (1) silicosis can impair the prolif-

erative phase of wound healing through the destruction of macrophages, which promote the inflammatory response and clear apoptotic cells [120], and (2) corticosteroid therapy for silicosis can additionally impair wound healing.

### 3.2.2.3 Acute Surgical Conditions

#### Acute Pancreatitis

A study of 17 pregnant women with acute pancreatitis in the third trimester (with 47% due to hyperlipidemia) found a high prevalence of IAH, with a mean IAP of 16.7 mmHg [121]. Two (12%) developed ACS, with organ dysfunction and a mean IAP of 21.7 mmHg.

#### Intestinal Obstruction

See Chap. 18.

#### Acute Appendicitis

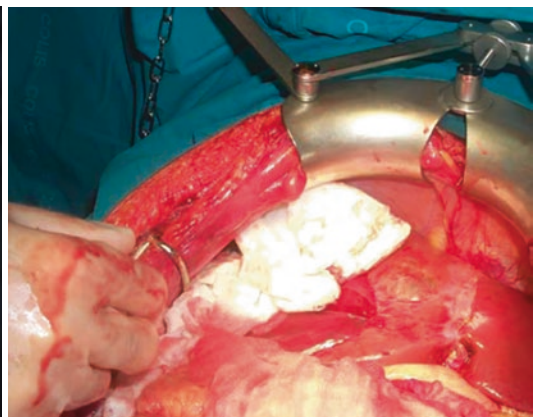
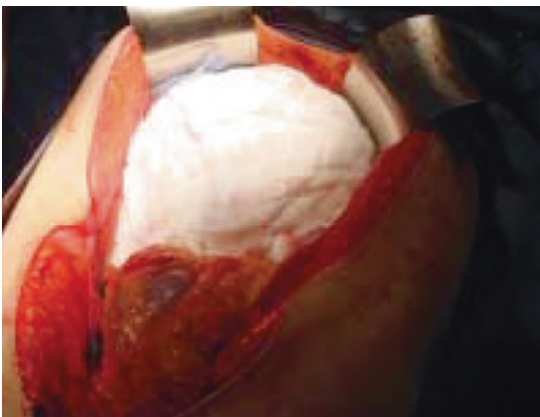
Acute appendicitis is the most common acute abdominal surgical condition during pregnancy. Therefore, although rare, the complications, such as diffuse peritonitis and subsequent IAH, are proportionally high [122, 123].

#### Spontaneous Hepatic Rupture

Spontaneous hepatic rupture in pregnancy with hemoperitoneum causes IAP. The condition is most commonly the result of preeclampsia, which is a cause of increased IAP [124]. The third factor that increases IAP is perihepatic packing (Fig. 3.7), a commonly used measure for temporary bleeding



**Fig. 3.6** Protrusion of a 28–30-week pregnant uterus through a large, 10-year unrepaired incisional hernia site. (Reproduced with permission from [113])



**Fig. 3.7** Perihepatic packing as a temporary treatment of spontaneous liver rupture in pregnancy. (Reproduced with permission from [124] under the CC BY 4.0 and Reproduced with permission from [125])

control when a hepatobiliary surgeon is unavailable [124, 126]. Simultaneously with perihepatic packing, CS is performed. Due to deranged coagulation, closure of the gravid uterus is commonly completed with pelvic packing, which also increases IAP [127]. In most published cases, IAP was not measured or not mentioned. One of the positive effects of lowering IAP is emergent CS.

### 3.3 Clinical Presentation

The diagnosis of peripartum ACS is challenging due to the lack of well-established normative pregnant values of IAP and the overlap of signs and symptoms between ACS and severe preeclampsia, such as oliguria and nonspecific abdominal pain [128]. Abdominal distension is always present. Percussion reveals intraperitoneal fluid or tympanism (drum-like distension) characteristic of bowel obstruction or paralytic ileus. BP differentiates between preeclampsia/eclampsia (elevated) and septic or hemorrhagic shock. BP should be checked every several hours or when the clinical condition deteriorates. Patients with elevated BP with HELLP syndrome can develop hepatic rupture with the hemoperitoneum resulting in a fall in BP [54].

A burst abdomen is easy to detect clinically as a possible consequence of IAH/ACS in pregnancy. The condition may manifest following straining or removal of the skin sutures. Patients often note a ‘ripping sensation’ or a feeling that ‘something has given way’. Impeding abdominal wall dehiscence is often preceded by the appearance of a salmon-pink serous discharge from the wound. Late presentation of the burst abdomen could result from the increased IAP and compression on the weakened abdominal wall from the inside, sometimes with surgical site infection. Large gravid uterus can be the only organ [113, 129] of evisceration (Fig. 3.6).

### 3.4 Diagnosis

Diagnostic workup should include the detection of IAP, IAH, and ACS and the underlying pathophysiologic process that leads to increased

IAP. Nonoperative (see Sect. 2.2.1) and operative conditions (see Sect. 2.2.2) should be searched. ACS is widely unrecognized because the routine measurement of IAP generally has not been accepted.

#### 3.4.1 Intra-abdominal Pressure Measurement

IAP measurement in obstetric patients who receive  $\geq 100$  mL/kg total resuscitation volume within 24 h is recommended [27].

While the clinical examination is inaccurate for detecting raised IAP, IAH, and ACS, the diagnosis should rely upon accurate serial or continuous IAP measurements [130]. Serial IAP measurements should occur every 4–6 h in patients at risk of IAH [27]. There is an increasing number of IAP measurement techniques.

*Trans-bladder measurement at end-expiration through a Foley catheter is the method of choice due to its simplicity and low cost. The level of the transducer should be placed at the mid-axillary line at the level of the iliac crest to obtain accurate measurements. (World Society of Abdominal Compartment Syndrome [28])*

Abdominal compartmentalization leads to significantly different IAP values depending on the measurement location. For example, in OHSS, after multiple abdominal operations and adhesions, there is a significant discrepancy with IAP measurements through the bladder and stomach [131]. The pelvic compartment syndrome is a part of the pathophysiology that includes the origin of IAP from the retroperitoneum.

### 3.4.2 Laboratory Findings

Hematocrit, hemoglobin, platelets, bilirubin, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase are diagnostic for HELLP syndrome [128]. Three times over normal upper levels, serum amylase and lipase levels indicate acute pancreatitis (see Chap. 17). For example, after transvaginal oocyte retrieval, the underlying intraperitoneal infection can result in an abscess, primary or secondary peritonitis [132]. Raised C-reactive protein levels and leukocytosis indicate an underlying infection. New-onset proteinuria indicates preeclampsia/eclampsia. Blood urea nitrogen and creatinine levels determine the severity of the acute renal failure.

Thromboelastography helps in the accurate correction of deranged coagulation [127].

### 3.4.3 Plain Chest X-Ray

Chest X-ray can reveal pulmonary edema or pleural effusion due to intra-abdominal pathology with IAH.

### 3.4.4 Abdominal Ultrasound

Transabdominal ultrasound can reveal a large quantity of free intraperitoneal fluid. It detects underlying pathologies, such as large polycystic ovaries in OHSS and acute pancreatitis (see Chap. 17). Transvaginal ultrasound better defines gynecologic causes of IAP.

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## 3.5 Treatment

Prevention of IAH is the best way to avoid end-organ dysfunction and the associated sequelae of ACS. The treatment goal for ACS is to decrease IAP through medical or surgical targeting of the forces affecting IAP. Management strategies have five categories: a decrease in intraluminal contents, a decrease in abdominal space-occupying lesions, improvement of abdominal compliance,

avoidance of fluid overload, and physiological support of organs [28]. Medical management is achieved with bowel decompression, fluid collection drainage, sedation/analgesia, neuromuscular blockade, limiting fluid administration, and diuresis/dialysis. However, the only definitive treatment for ACS is surgical decompression of the abdomen. Surgical decompression should proceed without delay if indicated, as medical interventions are often insufficient to treat ACS adequately [133]. When ACS is encountered in an obstetric patient, assessment of fetal viability adds additional management considerations. Urgent “therapeutic” delivery may become necessary if the condition of the mother or fetus acutely worsens.

The proposed management algorithm for peripartum IAH and ACS is presented in Fig. 3.8.

### 3.5.1 Nonoperative Treatment

#### 3.5.1.1 Nutrition

Nutrition is a key component in the recovery of patients following severe injury or abdominal sepsis. The open abdomen results in significant protein and nitrogen loss (up to 2 g/day) in the general population [134]. Failure to account for this may lead to malnutrition and poor outcomes. This is more pronounced in pregnancy due to the additional nutritional requirements of the fetus. Protein deficiencies are also a risk factor for abdominal wall dehiscence.

Enteral feeding does not increase the risk of ACS [135], and it is safe within 36 h (or within hemodynamic stabilization) of damage control laparotomy [136–138] in the general population. This concept has demonstrated increased fascial closure rates and decreased infectious complications with early enteral nutrition. This could be applied to the pregnant population.

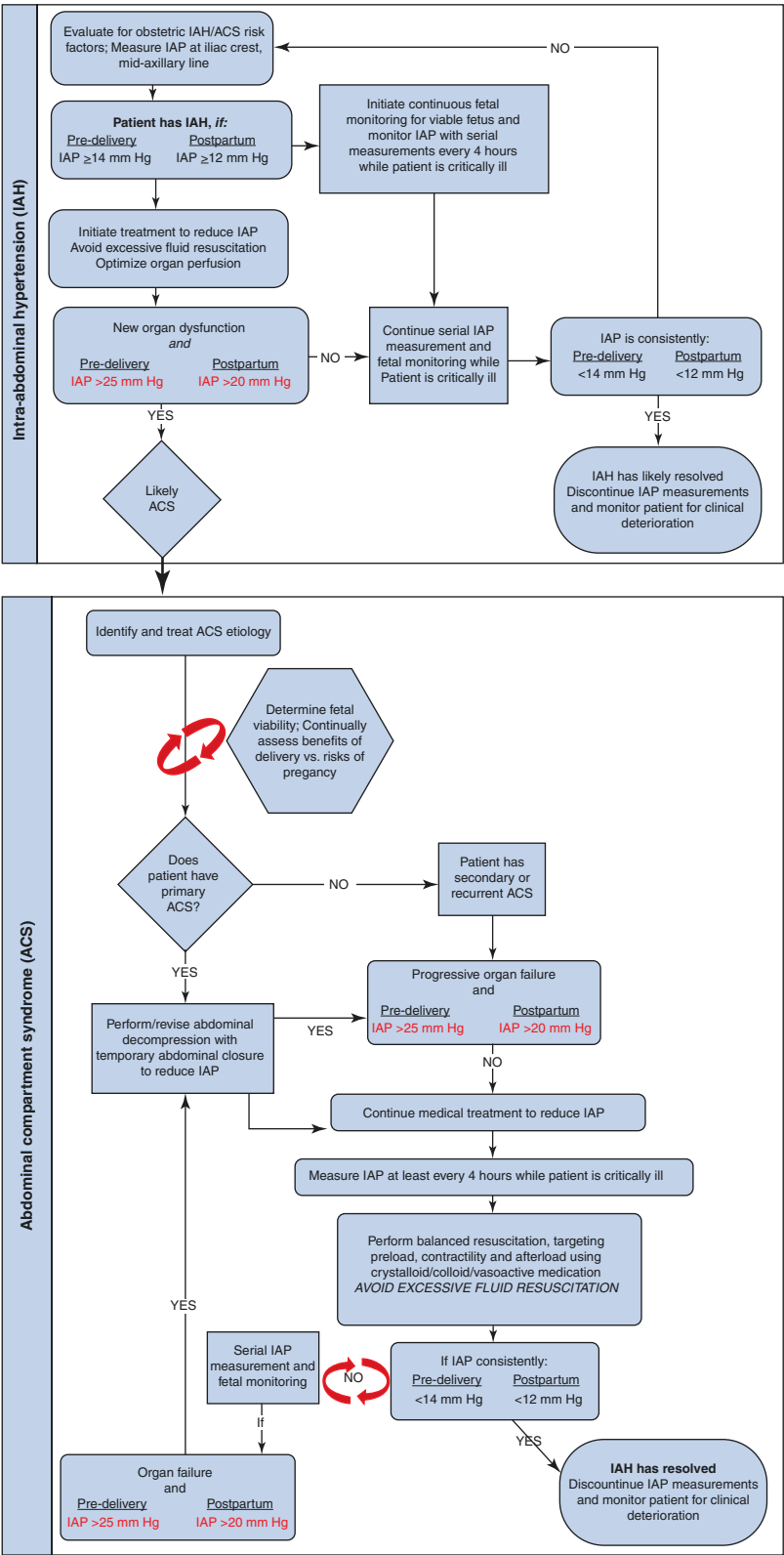
#### 3.5.1.2 Medical Treatment

##### Enteral Decompression

Enteral decompression is recommended with the liberal use of nasogastric or rectal tubes when the stomach or colon is dilated in IAH. Promotility



**Fig. 3.8** Proposed management algorithm for peripartum IAH and ACS. ACS abdominal compartment syndrome, IAH intra-abdominal hypertension, IAP intra-abdominal pressure. (Reproduced with permission from [27])



agents, such as metoclopramide (gastroparesis and small bowel ileus) or neostigmine (large bowel ileus), may be considered. Enteral nutrition can be minimized or interrupted in refractory IAH, considering the importance of nutrition in the critically ill. Consider enemas as a final step.

### **Evacuation of Intra-abdominal Lesions or Fluid**

Ultrasound or computed tomography can identify space-occupying lesions in the abdominal cavity. Fluid collections may be drained percutaneously or surgically. Paracentesis is indicated to relieve IAH or ACS from OHSS, primarily if a respiratory failure occurs [56, 58].

### **Management of the Underlying Disease**

Management of the underlying disease, such as OHSS, decreases the amount of intraperitoneal fluid and, therefore, IAP and IAH. Treatment ranges from conservative observation to intensive care admission with IAP monitoring and paracentesis to relieve ACS [56, 58]. Many consider polycystic ovaries the most important risk factor for OHSS [132]. Insulin resistance, hypothyroidism, and hyperprolactinemia are the most common causes of polycystic ovaries. After the endocrine disorders are addressed (levothyroxine and metformin), OHSS and IAP can be successfully treated [132].

### **Abdominal Wall Compliance Optimization**

Abdominal (wall) compliance is defined as the ease with which abdominal expansion can occur and is determined by the elasticity of the abdominal wall and diaphragm. Light sedation in the ICU increases abdominal compliance. The patient should be resting comfortably but easily arousable and able to follow simple commands. An analgesic agent should be prescribed first, followed by sedatives if required [139]. Deeper sedation may be needed to prevent forceful Valsalva maneuvers and evisceration. Analgesics and sedatives inhibit pain and awareness if the neuromuscular blockade is used. The association between benzodiazepine exposure in the first trimester and congenital anomalies is controversial and contradictory. A benzodiazepine infusion should not be withheld from a critically ill pregnant patient if needed for optimal care.

Neonatology personnel should be alerted to analgesia/sedatives in pregnant women. Epidural analgesia may also improve abdominal wall compliance and enhance peristalsis [140].

### **Optimization of Fluid Administration**

A negative fluid balance is desirable to decrease extravascular (lung) water and improve IAP in patients with IAH. The goal should be to achieve a neutral or negative fluid balance by day 3 [28]. Diuretics have not been studied in the ACS population, but furosemide may be safely used in pregnancy when indicated [141].

Resuscitation is characterized by permissive hypotension and limitation of crystalloid IV fluids and transfusing a 1:1:1 ratio of packed red blood cells to fresh frozen plasma to platelets to physiologically reconstitute whole blood [142]. The risk of ACS and associated mortality increases when the total resuscitation volume reaches more than 96 mL/kg (where most of the volume was given during the first 12 h) [143].

## **3.5.2 Operative Treatment**

Surgical intervention should proceed expeditiously when either maternal or fetal compromise cannot be reversed using conservative measures. Laparotomy alone does not indicate delivery; however, delivery of a viable fetus (>24 weeks estimated gestational age) may improve conditions for the mother and fetus. Conversely, the delivery of a nonviable fetus at decompressive laparotomy cannot be recommended because this increases blood loss and operative time.

Indications for laparo(s)tomy are [144, 145]:

- oliguria,
- hypotension,
- acidosis,
- intraoperative risk factors for IAH/ACS,
- abdominal sepsis,
- fetal compromise.



### 3.5.2.1 Source Control

Removal of the underlying cause, for example, as in Meigs' syndrome [65], has two therapeutic implications: (1) removal of the (functional) pathologic process itself and (2) the decrease of IAP due to the removal of bulky tumor/mass.

### 3.5.2.2 Planned Relaparotomy

As a rule, 24–48 h after the initial surgery for intra-abdominal sepsis or suspected organ vitality, the patient should be taken back to the operating room for reoperation. Reoperation should be performed in this time frame because (1) the abdominal exploration, lavage, drainage, and source control may be more difficult later due to the intraperitoneal adhesions and risks of bowel injury [146] and (2) the progress of organ ischemia, mostly bowel, does not result in ischemic perforation and (stercoral) peritonitis.

### 3.5.2.3 Decompression Laparotomy

The ideal temporary abdominal closure (TAC) method should [147, 148]:

- protect the abdominal contents,
- prevent evisceration,
- allow removal of infected or toxic fluid from the peritoneal cavity,
- prevent the formation of fistulas,
- avoid damage to the fascia,
- preserve the abdominal wall domain,
- make reoperation easy,
- safe,
- facilitate definitive closure,
- allow for postoperative fetal heart rate monitoring,
- allow space for uterine growth.

Intraoperatively, free intraperitoneal fluid or blood [54] should be evacuated. After several abdominal washouts with Ringer's lactate at 37–40 °C, the type of laparotomy closure is chosen [128]. Many different techniques of TAC have been introduced, but groups are small and heterogenous, making a comparison of techniques and outcomes difficult [149]. The advantages and disadvantages of different forms of TAC are summarized in Table 3.4.

Primary closure appears particularly challenging in the abdomen with the growing gravid uterus and low IAP requirements. It is nevertheless a key endpoint in a pregnant woman to protect the fetus and ensure a vaginal delivery. If the definitive fascial closure is not possible, another option may be skin-only closure to cover the exposed viscera and protect it, minimizing further injury to the exposed bowel. Ostomies should be placed as lateral as possible to be adequate [151].

Decompression laparotomy with various types of TAC (Fig. 3.9) is indicated for ACS, not the cause of ACS [128]. Delayed repair by bridging biological meshes in the open abdomen management has not been completely clarified. All guidelines and recommendations until 2021 do not discuss pregnant patients.

### Vacuum-Assisted Closure (VAC)

Only several cases are published involving negative pressure wound therapy or VAC on laparotomy wounds of gravid patients. There were no adverse effects on the fetus [117, 152, 153]. The initial value of negative pressure is not studied. Some started with less negative pressure (–75 mmHg), with an increase if no adverse effects were present (–100 mmHg) [117], while others started at maximum negative pressure (–125 mmHg) [153].

## 3.5.3 Obstetric Management

With ACS, the benefits of continuing pregnancy must be balanced against the risks of clinical deterioration to the mother and fetus. A low threshold for delivery is warranted while carefully monitoring for signs of compromised uteroplacental perfusion.

Therapeutic similarities (delivery of the fetus) were identified in the pattern of progressive multi-organ dysfunction in IAH and preeclampsia, resulting in abdominal decompression. The placenta is the mediating factor for the maternal systemic inflammatory response, and the delivery of the placenta could be the cure for preeclampsia. Therapeutic delivery as a treatment modality

**Table 3.4** Advantages and disadvantages of different types of temporary abdominal closure techniques [146, 150]

| Technique                                      | Equipment                                                                                 | Advantages                                                                                                                                       | Disadvantages                                                                                                                       |
|------------------------------------------------|-------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|
| Skin-only closure                              | Skin staples, towel clips, or sutures                                                     | Cheap, available, minimizes heat and fluid loss                                                                                                  | Damage to the skin, the risk of evisceration, no control of fluid loss, the incidence of ACS                                        |
| ‘Bogota’ bag                                   | Sterile 3 L saline bag cut and shaped and sutured to fascial edges                        | Cheap, available, minimizes heat and fluid loss                                                                                                  | Damage to the fascial edges, the risk of evisceration, and no control of fluid loss. Allows some assessment of intestinal viability |
| Opsite Sandwich Technique                      | Polyethylene sheet, Opsite dressings, abdominal packs, 2 suction drains, and wall suction | Cheap, available, minimizes heat and fluid loss; controlled and measurable                                                                       | Incomplete fluid control and need for available wall suction                                                                        |
| Absorbable mesh                                | Vicryl or similar mesh                                                                    | Absorbable mesh, infection resistance, protects from evisceration; can be skin grafted                                                           | The high rate of subsequent incisional herniation                                                                                   |
| Nonabsorbable mesh or Commercial ‘zipper’      | Commercial Whittman patch                                                                 | Abdominal reexploration is easy, maintains the abdominal domain, and gradual abdominal closure is possible                                       | Commercial equipment is required, and multiple trips to the operating theatre are usually required for closure                      |
| Vacuum-assisted closure (VAC)                  | Commercial equipment                                                                      | Prevents the loss of the abdominal domain, collects and monitors fluid loss, decreases ACS, and causes no damage to the skin or abdominal fascia | Expensive commercial equipment is required. Usually requires general anesthesia to change the VAC system                            |
| Abdominal reapproximation anchor System (ABRA) | Series of elastomers fixed to button anchors                                              | Continuous defect decrease due to constant tension on elastomers                                                                                 | Daily dressing changes                                                                                                              |

for the underlying cause is presented in various chapters depending on the cause.

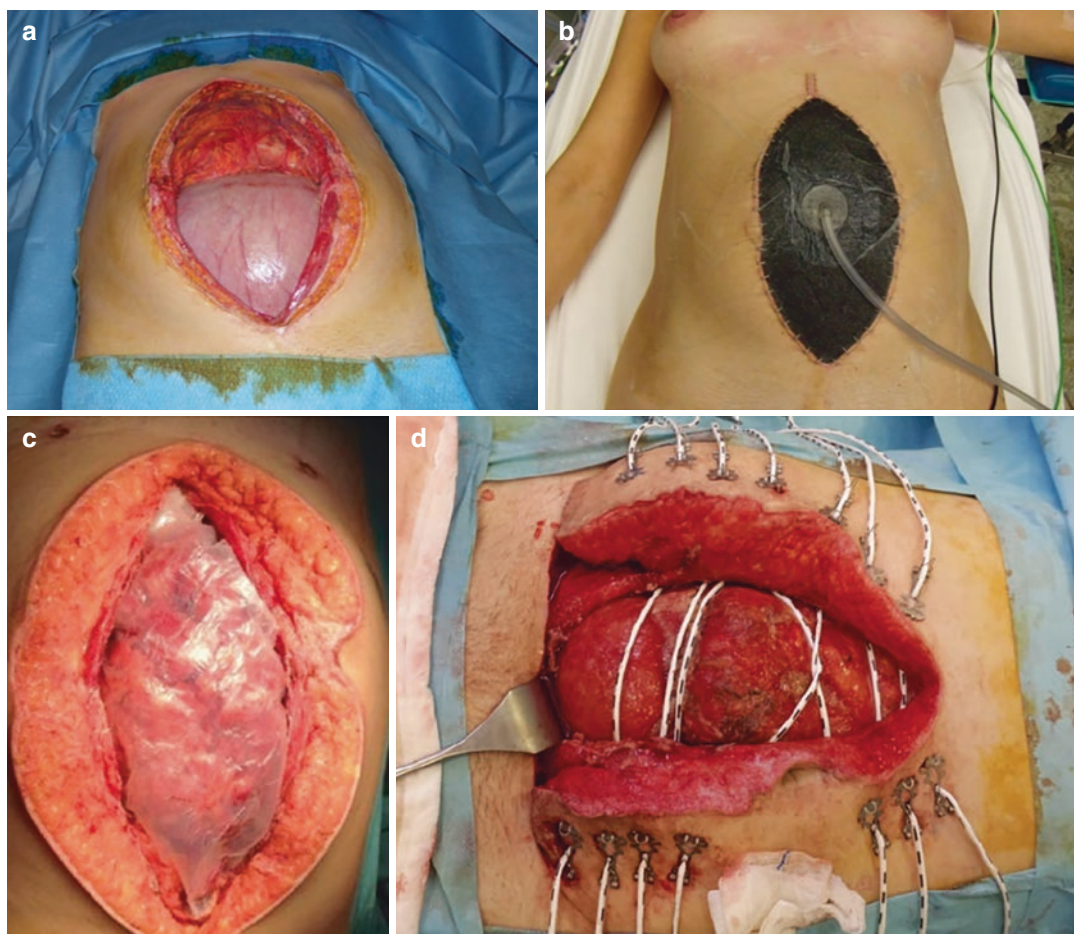
Indications for emergent CS are (1) obstetric, (2) uterus obstructs the operative field (mostly in trauma patients), and (3) maternal cardiopulmonary resuscitation (see Chap. 2). Fetal distress is an indication of the emergent CS of the viable fetus. The fetus is considered viable at a gestational age of 24 weeks. Fetal heart rate <100 bpm, prolonged deceleration for >1 min, or recurrent late decelerations prompt emergent delivery [154]. The survival of infants born at 23–25 weeks gestation was only 40% compared with those delivered at 26 weeks (80%) after maternal trauma. With spontaneous hepatic rupture, emergent CS is indicated. Due to underlying HELLP syndrome and secondary coagulopathy from massive bleeding, sutures on the uterus are sometimes not hemostatic. In such cases, pelvic packing is indicated. If unsuccessful, a total

abdominal hysterectomy should be performed [127].

The question remains whether expectant obstetric management is feasible when open abdominal management is deemed necessary for maternal care. Due to a small number of cases with different etiologies and weeks of pregnancy, conclusions cannot be drawn, but 75% (3/4 patients) had further normal pregnancies [122, 148, 150, 152].

### 3.5.3.1 Burst Abdomen

The management of a burst abdomen is difficult for both the surgeon and the obstetrician. Whether to close the abdomen and when and how to deliver the fetus depend on maternal and fetal factors. Therapeutic principles are the same as in the nonpregnant population, with the possibility of an additional procedure for lowering IAP and salvaging the fetus—CS (Fig. 3.10).



**Fig. 3.9** (a) The gravid uterus is in the inferior half of the laparotomy; (b) the open abdomen is 'closed' with vacuum-assisted closure. (Reproduced with permission from [152] under the CC BY 2.0); (c) the open abdomen

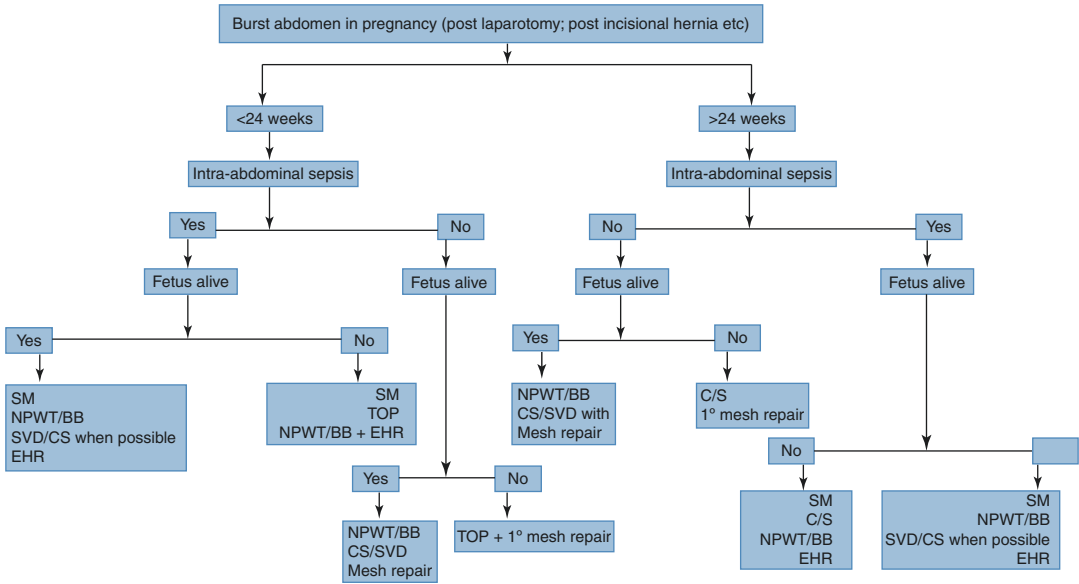
is temporarily closed with Bogota bag. (Reproduced with permission from [122]); (d) the technique of abdominal reapproximation anchor system. (Reproduced with permission from [150] under the CC BY 4.0)

### 3.5.3.2 Postpartum

At the postpartum IAP at various times following CS, the mean pressure remained below the cut-off value of 12 mmHg, within the non-IAH range. The IAP was  $7.4 \pm 3.8$  mmHg [20] when measured immediately after surgery;  $6.4 \pm 5.2$  mmHg [18] or 10.8 mmHg (95% CI: 4.5–18) at 1 h after surgery [30]; and  $9.8 \pm 3.0$  mmHg at 24 h [5]. Thus, postpartum values of IAP appear to be lower than those during pregnancy and outside the range for IAH, even for critically ill pregnant patients [9]. IAP values after delivery are similar in critically or noncritically ill obstetric patients, irrespective of risk factors for IAH seen in the ICU. Obese patients (BMI  $>30$  kg/m<sup>2</sup>) have sig-

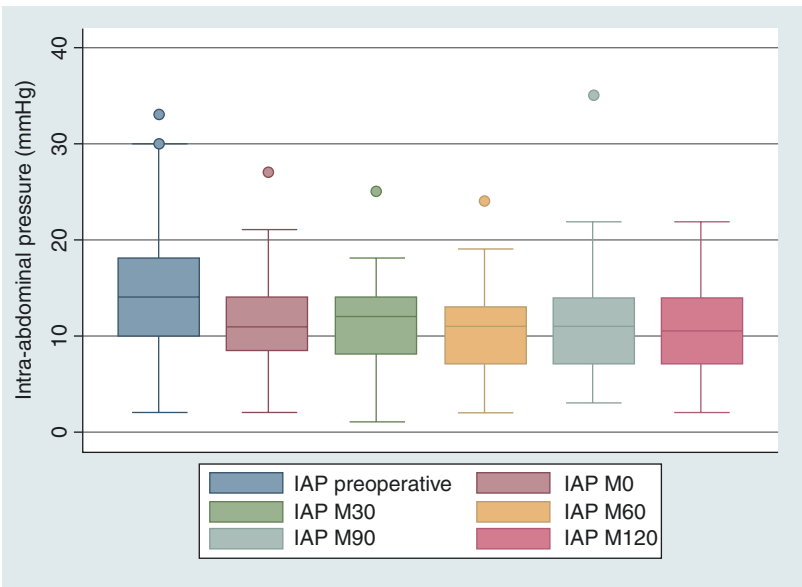
nificantly higher preoperative IAP levels than nonobese patients (15.7 vs. 12.4 mmHg, respectively) (Fig. 3.11). However, this difference also disappears after delivery [30], and values are by the standard value of IAP following uncomplicated abdominal surgery (10–15 mmHg) [66, 155]. Many factors have been described to explain this physiological increase after surgery, but the two main factors in obstetrics are the persistent increase in uterine size and the CS itself.

Every pregnant woman admitted to ICU after delivery should be monitored for IAP.



**Fig. 3.10** Management algorithm for burst abdomen in pregnancy. *SVD* spontaneous vaginal delivery, *NPWT* negative pressure wound therapy, *CS* cesarean section, *TOP* termination of pregnancy, *SM* surgical management involves laparotomy and peritoneal lavage if required, *BB* bogota bag, *EHR* elective hernia repair. (Reproduced with permission from [118])

**Fig. 3.11** Intra-abdominal pressure before Cesarean section (preoperative) and postoperative (every 30 min during 2 h). (Reproduced with permission from [30] under the CC Attribution Licence)



### 3.6 Prognosis

#### 3.6.1 Maternal Outcome

The maternal outcome depends on:

- the severity and duration of IAH/ACS,
- the cause of increased IAP,
- normalization of IAP after delivery.

Despite the presence of risk factors for IAH in ICU obstetric patients, the prevalence of IAH (IAP >12 mmHg) was only 6%, while 66% of patients had IAP 8–11 mmHg. Interestingly, this is much lower than for mixed, nonpregnant populations of critically ill patients in the ICU (19–80%) [9].

The usual IAP may be slightly higher in critically ill obstetric patients than in mixed populations of critically ill patients. Nevertheless, IAP does not affect organ function depicted by the SOFA score, and the low prevalence of IAH prevented the evaluation of affected organ dysfunction [9]. The prevalence of IAH was 75% in pregnant and 0% in postpartum patients.

Following delivery, a fall in IAP is associated with better survival [9].

##### 3.6.1.1 Burst Abdomen

Various methods for (temporary) closure of burst abdomen in pregnancy were used: two cases with negative pressure wound therapy [117, 153], one with the mesh [114] and one with Bogota bag [118]. Maternal mortality was 0%.

##### 3.6.1.2 Acute Pancreatitis

The development of IAH/ACS among patients with severe acute pancreatitis in the general population is a strong predictor of mortality up to 49% [156]. A study of 17 pregnant women with acute pancreatitis in the third trimester (47% due to hyperlipidemia) found a high prevalence of IAH, with a mean IAP of 16.7 mmHg [121]. Two (12%) developed ACS, with organ dysfunction

and a mean IAP of 21.7 mmHg. Maternal mortality was 0% [121, 150].

#### 3.6.2 Fetal Outcome

##### 3.6.2.1 Burst Abdomen

Fetal mortality depends on (1) the gravid uterus incarceration at presentation and (2) gestation of less than 24 weeks [114, 117, 118, 153].

##### 3.6.2.2 Acute Pancreatitis

A study of 17 pregnant women with acute pancreatitis in the third trimester (with 47% due to hyperlipidemia) found a high prevalence of IAH, with a mean IAP of 16.7 mmHg [121]. Two (12%) developed ACS, with organ dysfunction and a mean IAP of 21.7 mmHg. Fetal mortality was 31.2%, and higher maternal IAP correlated with higher fetal mortality.

##### 3.6.2.3 Acute Appendicitis

Both patients were in the second trimester. Neither received tocolysis, and neither went to preterm labor [122, 123]. Deliveries were uneventful, and both children had normal development.

##### 3.6.2.4 Obesity

High IAP may compress the maternal aorta and uterine arteries, reducing uterine perfusion pressure and fetoplacental insufficiency. The higher predelivery IAP was associated with lower newborn NACS (Neurologic and Adaptive Capacity) scores. This association was found most often among women with Class III obesity (BMI  $\geq 40$  kg/m<sup>2</sup>) who received spinal anesthesia [157].

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# Acute Abdomen-Induced Preterm Labor

## 4

### Abstract

The specific issue with acute abdomen during pregnancy is that many underlying conditions result in inflammation and infection, which raise prostaglandin levels, which are crucial for normal labor progress. Therefore it is mandatory to stop the increased preterm production of prostaglandins. The only solution is early diagnosis and treatment of acute abdominal conditions during pregnancy. In addition to inflammation, abdominal trauma is also an issue. It can cause placental abruption and preterm labor. In addition to these two most common groups of the acute abdomen during pregnancy, other important topics are discussed. These include maternal and fetal stress as a result of any cause of acute abdomen during pregnancy and the problem of adequate perioperative nutrition. Inadequate maternal nutrition results in diseases with a prolonged course before therapeutic interventions such as conservatively treated acute cholecystitis or acute pancreatitis. Prolonged inadequate postoperative nutrition is seen after many surgical procedures, especially those requiring bowel resections or reoperations. Therefore underlying pathology should be diagnosed and treated early in the course of the disease. Additional measures for detecting and preventing preterm labor should be instituted as early as possible.

### 4.1 Definitions

*Preterm labor* (PTL) is a process of regular contractions accompanied by the cervical change before 37 completed weeks of gestation. PTL can be:

- Induced for maternal or fetal indications (drug-induced or delivery by elective or emergent Cesarean section (CS)),
- Spontaneous PTL:
  - cervical dilation and intact membranes,
  - preterm premature rupture of the membranes (PPROM).

PPROM is defined as the spontaneous rupture of the membranes at less than 37 weeks' gestation at least 1 h before the onset of contractions. About 30–35% of PTLs are indicated, 40–45% follow spontaneous PTL, and 25–30% follow PPROM [1, 2].

*Preterm birth* (PTB) is subdivided into extremely preterm (<28 weeks), very preterm (28–32 weeks), and moderate to late PTB (32–36 weeks) [3]. Today, births can occur as early as 16 weeks of gestation, making the line between spontaneous abortion and spontaneous PTB more challenging.

PTL can be initiated by multiple mechanisms—infection/inflammation, uteroplacental ischemia or bleeding, uterine trauma, uterine overdistension, or stress [4].

## 4.2 Physiology of Labor

Human labor is an inflammatory, three-step process characterized by uterine contractility, cervical ripening, and membrane activation/rupture [5]. The fundamental difference between the term labor and PTL is that the former results from the “physiologic activation” of this common pathway. In contrast, PTL results from either early idiopathic activation of the normal labor or disease process (“pathologic activation”) that activates one or more of the components of the common pathway [5]. Monocytes and neutrophils are primed in the peripheral blood associated with term and PTL [6]. These cells infiltrate the human myometrium and cervix during spontaneous term labor, which is associated with a significant increase in interleukin (IL-1 $\beta$ , IL-6, and IL-8) gene expression [7].

The *common pathway of parturition* includes the anatomic, biochemical, immunologic, endocrinologic, and clinical events in the mother and fetus at term or PTL. Fetal cortisol is central to labor initiation [8]. As parturition nears, the fetal-adrenal axis becomes more sensitive to the adrenocorticotrophic hormone, increasing cortisol secretion. Fetal cortisol stimulates placental 17 $\alpha$ -hydroxylase activity, decreasing progesterone secretion and increasing estrogen production. The reversal in the estrogen/progesterone ratio results in increased prostaglandin formation, initiating a cascade of events resulting in labor (see Sect. 4.2.4). During pregnancy, the uterus is maintained in a relatively quiescent state through the separate or combined autocrine–paracrine actions of inhibitors such as progesterone, prostacyclin (PGI<sub>2</sub>), relaxin, parathyroid hormone-related peptide, calcitonin gene-related peptide, adrenomedullin, vasoactive intestinal peptide, nitric oxide, and corticotrophin-releasing hormone, which may inhibit and stimulate uterine contractility [9].

Activation of the uterine components of the common pathway of parturition may be synchronous or asynchronous. *Synchronous activation* results in clinical spontaneous PTL. *Asynchronous activation* results in (1) predominant activation of the membranes that leads to PPROM, (2) of the cervix to cervical insufficiency, and (3) that of the

myometrium to preterm uterine contractions without cervical change or rupture of membranes.

### 4.2.1 Myometrial Contractility

Increased cell-to-cell communication is responsible for the effectiveness of myometrial contractility during labor. Gap junctions develop in the myometrium just before labor and disappear shortly after delivery [10, 11]. Gap junction formation and the expression of the gap junction protein, connexin-43, in human myometrium are similar in both term labor and PTL [12–14]. The appearance of gap junctions and increased expression of connexin-43 are part of the molecular and cellular events responsible for switching from contractures to contractions before the onset of parturition. Estrogen, progesterone, and prostaglandins regulate gap junction formation and influence the expression of connexin-43 [15–17]. Connexin-43 and other distinct contraction-associated proteins are characteristic of this phase of parturition [18–20].  $\alpha$ -actin was expressed in the myometrium in early pregnancy, whereas  $\gamma$ -actin was highly expressed by the myometrium with a contractile phenotype.

Myometrial phenotype programming [21] and sequential phenotypic changes start from an *early proliferative phase*. It is characterized by bromodeoxyuridine incorporation, the proliferating cell nuclear antigen expression level, increased IGF-I signaling, and the expression of anti-apoptosis factors such as Bcl-2 [21]. An intermediate synthetic phase is characterized by increased cell size and synthesis/deposition of the interstitial matrix that forms the ground substance of the myometrium [22–24]. A *late contractile phase* is characterized by the upregulation of contraction-associated proteins, oxytocin, and prostaglandin receptors in which the cells are committed to labor [14, 25, 26]. This phenotypic programming is accomplished through two separate but integrated pathways: an endocrine cascade comprising the fetal hypothalamic-pituitary-adrenal-placental axis and a mechanical pathway in which fetal growth imposes tension on the uter-



ine wall [9]. Abnormal myometrial stretch (i.e., polyhydramnios, multiple gestations) promotes the expression of gap junction proteins, oxytocin receptors, and prostaglandins in the amnion myometrium and cervical cells [27]. These alterations promote uterine activity and the degradation of the extracellular matrix, thereby facilitating cervical ripening and ROM.

### 4.2.2 Cervical Remodeling

The changes in the cervix include: (1) softening, (2) ripening, (3) dilatation, and (4) postpartum repair [28]. The molecular and cellular basis for cervical remodeling during pregnancy and parturition primarily depends on regulating extracellular matrix components [28, 29]. Leukocytosis in the cervix responds to increasing local levels of estrogens derived from fetal adrenal precursors. This results in the release of metalloproteinases/collagenases, driving cervical ripening and dilatation. It facilitates access by cervicovaginal microflora to the surface of the membranes covering the cervical os, furthering the inflammatory response in the amniotic cavity. Hyaluronidase activity increases in the cervix due to functional progesterone withdrawal, degrading hyaluronan leading to disaggregation of polymers, inflammatory activation, and cervical ripening [30]. The softening of the cervix begins in early pregnancy. The tensile strength of the softened cervix appears to be maintained by an increase in collagen synthesis and growth of the cervix. Cervical ripening is characterized by a decreased concentration of collagen and the dispersion of collagen fibrils. The latter has been attributed to glycosaminoglycans, such as decorin and hyaluronan, which promote the hydration of cervical tissue and dispersion of collagen fibers [29]. Dilation of the cervix is an inflammatory phenomenon with an influx of macrophages, neutrophils, and matrix degradation [31, 32]. Chemokines such as IL-8 [33, 34] and S100 proteins [35, 36] attract inflammatory cells, which, in turn, release pro-inflammatory cytokines, including IL-1 $\beta$  [37, 38] and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) [36], which can activate the nuclear factor (NF)- $\kappa$ B signaling

pathway. NF- $\kappa$ B can block progesterone receptor-mediated actions [39]. Progesterone has been implicated in regulating cervical remodeling because the administration of antiprogestins in the mid-trimester and, at term, induces cervical ripening [28, 40, 41].

### 4.2.3 Decidual/Membrane Activation

During pregnancy, the chorioamniotic membranes fuse with the decidua. In preparation for delivery, biochemical events lead to separation and postpartum expulsion of the membranes. Fibronectins are a family of essential extracellular matrix proteins. The degradation of a heavily glycosylated form of cellular fibronectin—fetal fibronectin—present at the chorionic-decidual interface leads to its release into cervical and vaginal secretions immediately before term or PTL [42–44].

Enzymatic activity of matrix metalloproteinases (MMPs) and other proteases has been implicated in the process of rupture of membranes and parturition with intact membranes (with and without infection) [45, 46]. The precise decidual/membrane activation mechanism remains unknown, but extracellular matrix-degrading enzymes, such as the MMPs and elastase, have a role. There is increased availability of MMP-1 (interstitial collagenase) [47], MMP-8 (neutrophil collagenase) [47], MMP-9 (gelatinase-B) [48], and neutrophil elastase [49] in the amniotic fluid of women with PPRM, compared with women in PTL with intact membranes. Plasmin has also been implicated [44] because it can degrade type III collagen, fibronectin, and laminin [50]. A role for tissue inhibitors of MMPs (TIMPs) has also been postulated.

### 4.2.4 Prostaglandins and Parturition

Prostaglandins are the key mediators for the onset of labor [51]. They induce myometrial contractility [51, 52], changes in extracellular matrix

metabolism associated with cervical ripening [53, 54], and decidual/membrane activation. Both COX-1 and COX-2 are present within the pregnant uterus. The expression of COX-1 remains constant throughout gestation. However, there is an exponential rise in COX-2 activity throughout gestation in the fetal membranes, chorion-decidua, and myometrium, with most of the increase occurring before the onset of labor. The fetal membranes are a major source of prostaglandin synthesis. Prostaglandin synthesis in fetal membrane explants is suppressed by COX-2-specific inhibitors but not by COX-1-specific inhibitors. This demonstrates the importance of COX-2 in the production of intrauterine prostaglandins. This increase in amniotic COX-2 activity is accompanied by decreased expression of the prostaglandin-metabolizing enzyme, 15-hydroxy-prostaglandin dehydrogenase (PGDH), in the chorion. Progesterone promotes PGDH expression through its effect on the progesterone receptor (PR) B. This would allow prostaglandins produced in the amnion to traverse the chorion and reach the myometrium, where they can stimulate smooth muscle contractions [55]. The biochemical mechanisms by which prostaglandins activate the common pathway of parturition are the following: (1) prostaglandins directly promote uterine contractions by increasing sarcoplasmic and transmembrane calcium fluxes and through increased transcription of oxytocin receptors, connexin-43 (gap junctions), and the prostaglandin receptors EP1 through EP4 and FP27 [56, 57], (2) prostaglandins induce synthesis of MMPs by fetal membranes and cells within the uterine cervix (as noted, MMPs have been implicated in the mechanisms of membrane rupture and also in cervical ripening) [58, 59]; and (3) prostaglandin E2 (PGE2) and PGF2 $\alpha$  increase the ratio of expression of the PR-A and PR-B isoforms [60]. Progesterone interaction with PR-B inhibits myometrial ER $\alpha$  expression causing the myometrium to be refractory to estrogens. As gestation progresses, the increase in myometrial PR-A expression decreases PR-B activity and eliminates the PR-B-mediated inhibition of ER $\alpha$  expression [61]. Changes in progesterone recep-

tor ratio induce a functional progesterone withdrawal because, unlike other mammalian species, circulating progesterone levels do not decrease during the onset of labor.

### 4.3 Etiopathogenesis of Preterm Labor

Spontaneous PTL can result from (1) maternal conditions, (2) fetal conditions, and (3) placental conditions. These conditions could be infective or noninfective. Intra-amniotic infections (IAI) are present in ~50% of all pregnancies that result in PTB, and the earlier the gestational age at delivery, the higher the frequency of IAI [62]. This chapter will concentrate on the influence of localized/diffuse peritonitis and abdominal trauma on PTL. Localized/diffuse peritonitis synergistically increases the rate of PTL with other factors. Risk factors for PPRM are generally similar to those for spontaneous PTL with intact membranes, although infections and tobacco exposure are essential [63]. Oxidative stress-induced fetal membrane senescence contributes to inflammation [64]. In response to oxidative stress-inducing risk factors, premature senescence activation and inflammation can predispose to PTB and PPRM [65].

Spontaneous PTLs utilize a common biochemical pathway (see Sect. 4.3.4), employed by each pathogenic pathway with specific genetic or epidemiologic risk factors and unique biochemical triggers. Mechanical uterus stretching from multifetal gestations and cervical insufficiency is outside this book's scope.

#### 4.3.1 Inflammation

The amniotic cavity is sterile for bacteria in 99% of cases. It contains antimicrobial properties—a low number of WBC, lactoferrin, and other proteins implicated in fetal host defense mechanisms [66]. With IAI, WBC rise in the amniotic cavity [67]. The most abundant WBC in the amniotic cavity are the neutrophils in both types of inflammatory processes—initiated by either intra-



amniotic microorganisms or danger signals derived from necrosis or cellular stress (i.e., sterile IAI) [67]. Single amniocentesis shows that 40% of intra-amniotic neutrophils are mostly fetal, >30% predominantly maternal, and 20% a mixture of fetal and maternal neutrophils [68]. Extreme PTL is present with predominantly amniotic fluid neutrophils of fetal or mixed origin (71.5% and 66.7%, respectively). All women with predominantly amniotic fluid neutrophils of maternal origin had a term or late PTL [68]. Fetal neutrophils are predominant in the amniotic cavity of women with IAI or (sterile) inflammation with resultant PTL. Fetal neutrophils possibly invade the amniotic cavity by migrating from the fetal vasculature of a chorionic plate of the fetus [69]. An amniotic fluid containing predominantly fetal neutrophils did not show maternal or fetal inflammatory responses in the placental tissues [68]. Neutrophils migrate from the maternal vasculature into the amniotic fluid of women with IAI to participate in the host defense mechanisms against pathogens invading the amniotic cavity [68].

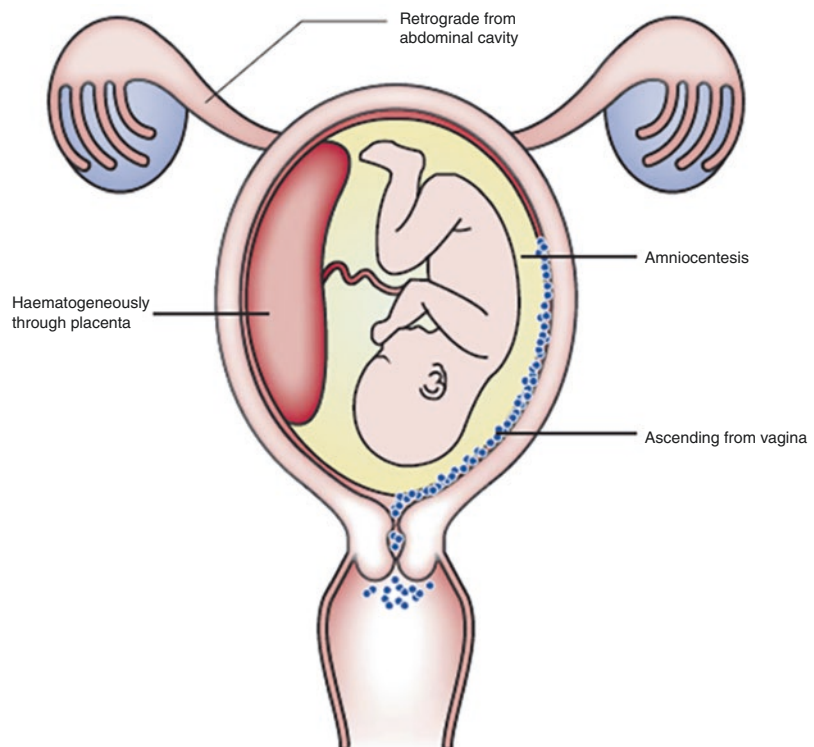
Infection is a frequent and essential cause of PTL. Microorganisms can gain access to the amniotic cavity by (Fig. 4.1):

- ascending from the vagina and the cervix,
- by hematogenous dissemination through the placenta,
- introduction at the time of invasive procedures,
- by retrograde spread through the Fallopian tubes,
- combined access.

Evidence for causality includes:

- intrauterine infection or systemic presence of microbial products (bacterial endotoxin),
- extrauterine maternal infections (periodontal disease [70], malaria, pyelonephritis, and pneumonia),
- subclinical intrauterine infections (histologic chorioamnionitis) [71],
- intra-amniotic infection or inflammation (defined as an elevation of amniotic fluid con-

**Fig. 4.1** Potential routes of intrauterine infection. (Reproduced with permission from [4])



centrations of pro-inflammatory cytokines and matrix-degrading enzymes in the mid-trimester) [72],

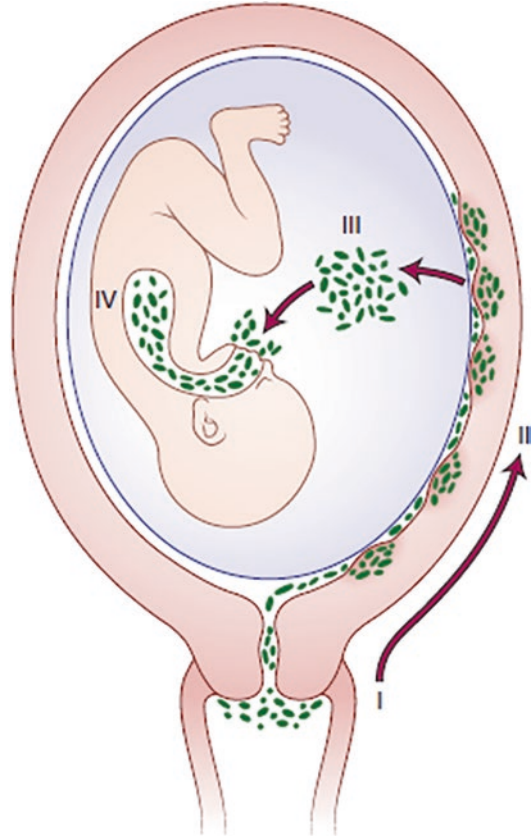
- antibiotic treatment of ascending intrauterine infections can prevent PTL in experimental models of chorioamnionitis,
- treatment of asymptomatic bacteriuria prevents PTL.

The extent of bacterial colonization, route of infection, and bacterial stimulatory capacity are important in activating maternal and fetal pro-inflammatory signaling cascades. Most studies are based on genital tract infections causing intrauterine infection, without large studies on the pathophysiology and microbiology of peritonitis-induced PTL.

Intrauterine inflammation is associated with approximately 25–40% of all PTLs [4, 73] and 79% of extreme PTB tested [74]. This is a conservative estimate due to the difficulty of detecting chorioamnionitis using conventional culture techniques [4]. Also, women with a PCR-positive amniotic fluid for *U. urealyticum* but a negative culture have similar rates of PTL as women with positive cultures for the same microorganism [75]. Furthermore, since the rate of microbial colonization of the chorioamnion is twice that seen in the amniotic cavity, rates of intrauterine infection based only on amniotic fluid cultures substantially underestimate the level of association [76].

#### 4.3.1.1 Ascending Intrauterine Infection

Ascending intrauterine infection has four stages (Fig. 4.2). *Stage I* involves changing the vaginal and cervical microbial flora. Some forms of bacterial vaginosis may be an early manifestation of stage I. Once microorganisms gain access to the intrauterine cavity, they reside in the decidua (*Stage II*). A localized inflammatory reaction leads to deciduitis. Microorganisms may then reside in the chorion and amnion. The infection may invade the fetal vessels (choriovasculitis/choriodecidualitis) or proceed through the amnion (amnionitis) into the amniotic cavity, leading to the microbial invasion of the amniotic cavity or



**Fig. 4.2** The pathway of ascending intrauterine infection. *Stage I* refers to a change in the vagina or cervix microbial flora. In *Stage II*, microorganisms are between the amnion and chorion. *Stage III* represents intra-amniotic infection, and *Stage IV* is a fetal invasion. (Reproduced with permission from [78] and modified)

an IAI (*Stage III*). Rupture of the membranes is not a prerequisite for IAI because microorganisms can cross intact membranes [77]. Once in the amniotic cavity, the bacteria may access the fetus through different ports of entry (*Stage IV*). Aspiration of the infected fluid by the fetus may lead to congenital pneumonia. Otitis and conjunctivitis may occur by the direct spread of microorganisms from the infected amniotic fluid. Funisitis results from the spread of infection to and through the umbilical cord. Seeding from these sites to fetal circulation may result in fetal bacteremia and sepsis.

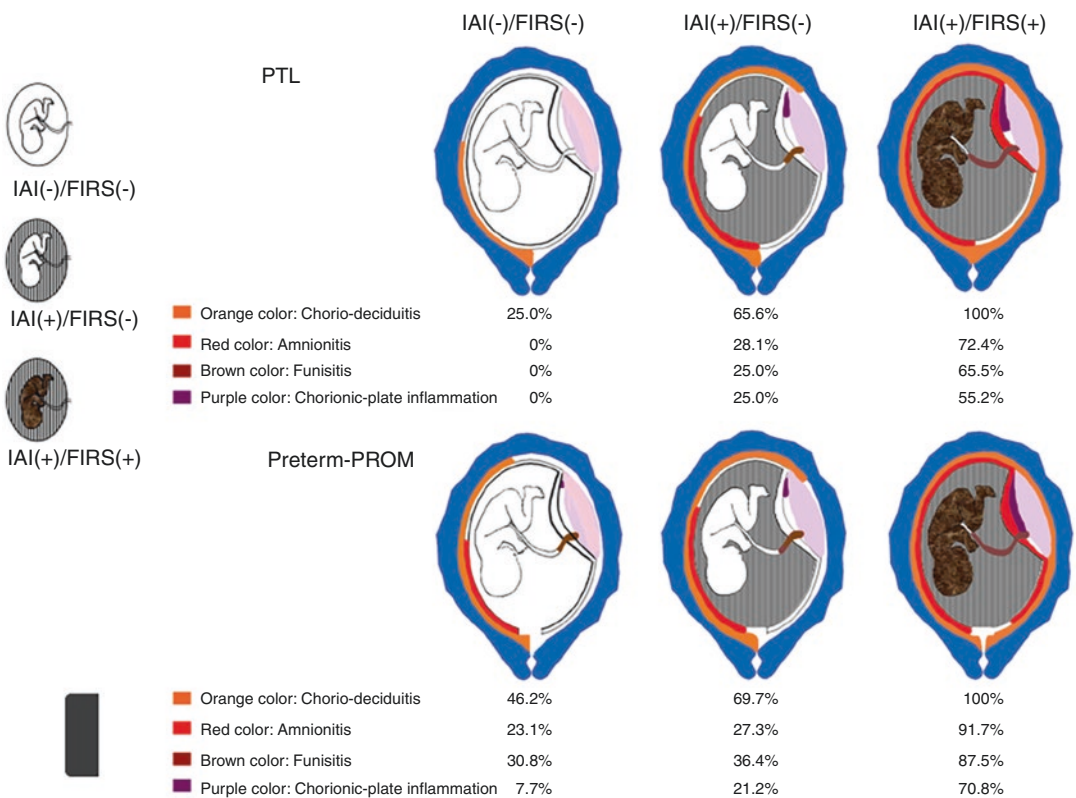
IAI and FIRS are more severe in PTL than in PPROM, despite less common IAI in PTL than in PPROM in the most advanced stage of ascending

intrauterine infection—funisitis [79]. Inflammation is not detected in any compartment (i.e., amnion, chorionic plate, or umbilical cord) except the choriodecidua in the IAI(−)/FIRS(−) group with PTL, while present in all compartments in the IAI(−)/FIRS(−) group with PPROM. Also, IAI(+)/FIRS(−) group has a significantly higher frequency of inflammation in each compartment than the IAI(−)/FIRS(−) group in PTL but not PPROM (Fig. 4.3) [80].

Microbial invasion of the amniotic cavity or chorioamnion may be caused by direct accessibility without substantial involvement of choriodecidua by cervicovaginal microorganisms with ROM. PPROM would be more likely to show neutrophils exiting from decidual postcapillary venules and migrating to amnion in response to microorganisms that have already entered the AF or chorioamnion than PTL even

before cytokine responses in AF become elevated [80].

Microbial invasion of the amniotic cavity (MIAC) is present in 12.8% of women with PTL [81] and 21–32% with PPROM [81, 82]. Most (83%) are complicated by microbial-associated IAI. Sterile IAI is responsible for a small proportion of pregnancies complicated by IAI (17–33%). The majority of women with PPROM have sterile inflammation [82, 83]. Different gestational week ranges and IL-6 cut-off values for the definition of IAI were used. The amniotic cavity microbial invasion was detected in 51% of patients with acute cervical insufficiency. Patients with MIAC are more likely to have PTL, spontaneous ROM, and clinical chorioamnionitis than those with sterile amniotic fluid. The most common organisms found in the amniotic fluid are genital mycoplasmas. It is believed that ascend-



**Fig. 4.3** A schematic representation of the histotopographic distribution of involved compartments, according to the presence or absence of IAI or FIRS. The colored area of each compartment (i.e., choriodecidua, amnion, umbilical cord, and chorionic plate) means the proportion of cases with inflammation. *IAI* intra-amniotic infection, *FIRS* fetal systemic inflammatory response. (Reproduced with permission from [80])

ing infection is the most common source of microbial invasion of the amniotic cavity, although transplacental infections may also occur. The lower the gestational age at which a patient presents with PTL and PPROM, the higher the frequency of MIAC. Moreover, many of these infections appeared to be chronic and were detected in women having mid-trimester amniocentesis for genetic indications. Bacterial products such as endotoxin have also been detected in the amniotic cavity of women with PTL and PPROM. Endotoxin has powerful pro-inflammatory effects in maternal and fetal tissues. While PPROM near term likely results mainly from the physiologic processes, PPROM remote from term has been associated with several pathologic processes, especially infection and inflammation, membrane stretch, and local tissue hypoxia.

PPROM in ascending infection is due to bacterial proteases (collagenases and phospholipases) that cause membrane weakening. Ascending bacterial colonization can also cause a local inflammatory response, including the production of cytokines, prostaglandins, and metalloproteases which cause membrane degradation and weakening.

Microorganisms are detected by the innate components of the immune system: (1) the soluble pattern recognition receptors (PRRs), lectin, and CRP; (2) transmembrane PRRs, which include scavenger receptors, C-type lectins, and Toll-like receptors (TLRs); and (3) intracellular PRRs, including Nod1 and Nod2, retinoic-induced gene type 1, and melanoma differentiation-associated protein 5, which mediate recognition of intracellular pathogens (e.g., viruses). The best-studied PRRs are the TLRs. Ligation of TLR results in the activation of NF- $\kappa$ B, which, in turn, leads to the production of cytokines, chemokines, and antimicrobial peptides. Because TLRs are crucial for recognizing microorganisms, defective signaling through this pathway could be anticipated to impair bacteria-induced PTL. Consistent with this, a strain of mice bearing a spontaneous mutation for TLR-4 was less likely to deliver preterm after intrauterine inoculation of heat-killed bacteria or adminis-

tration of lipopolysaccharide than wild-type mice. In pregnant women, TLR-2 and TLR-4 are expressed in the amniotic epithelium and decidua. Moreover, spontaneous labor that occurs at term or preterm and is complicated by histologic evidence of chorioamnionitis, regardless of the membrane status (intact or ruptured), is associated with increased mRNA expression of TLR-2 and TLR-4 in the chorioamniotic membranes. These observations suggest that the innate immune system plays a role in parturition.

#### 4.3.1.2 Hematogenous Spread to the Placenta

Few bacteria are capable of placental and fetal infections (*Brucella* spp, *C. burnetii*, *L. monocytogenes*, *M. tuberculosis*, and *T. pallidum*), and even for these, the maternal infection does not result in placental or fetal infection [84]

Common distant infective focuses include periodontal respiratory disease with several hypothetical models for the contribution in PTL. *Direct pathway*: periodontal bacteria or their pathogenic products disseminate to the placenta, initiating a distant infection or triggering a local inflammatory response that elevates inflammatory cytokines and mediators. *Indirect pathway*: inflammatory cytokines and mediators produced by gingiva in response to periodontal pathogens enter the blood circulation and reach (1) the placenta and enhance the accumulation of larger amounts of these mediators, (2) the liver, where they stimulate a systemic inflammatory response by the production of acute-phase reactants. These products gain access to blood circulation and may enter the placenta exacerbating intrauterine inflammation. During pregnancy, elevated levels of estrogens and progesterone increase vascular permeability in the gingiva, and bacteria or their products diffuse through the tissues more easily [85].

Pro-inflammatory cytokines in the maternal circulation and transient bacteremia may induce systemic inflammation by stimulating the production of acute-phase reactants, such as CRP and fibrinogen. Elevated levels of plasma CRP could amplify the inflammatory response at the feto-placental interface through complement

activation. Thus, elevated CRP could initiate PTL or PPROM [86] and other obstetric complications such as IUGR [87]. The difference between acute (PTL or PPROM) and chronic obstetric complications (IUGR, LBW) could depend on (1) the infective burden (diffuse stercoral peritonitis or periodontal disease), (2) different fetomaternal unit compartment involvement, and (3) different inflammation pathway activation. Finally, this could result in differences in maximal acute-phase reactant levels, increasing obstetric complication rates. Also, several loci of infection could be present simultaneously, stimulating inflammation via the hematogenous route (i.e., periodontal disease and acute respiratory disease) or different routes, for example, hematogenous and ascending route (i.e., asymptomatic bacteriuria, acute respiratory disease, and bacterial vaginosis). Combined infections/inflammations can result in higher serum acute-phase reactant levels than a single infective locus.

#### 4.3.1.3 Intraperitoneal Infection

The extrauterine intraperitoneal infection reaches the fetal circulation by placental transmission. Concomitant IAI could be present. There are no studies in this field, and only hypotheses can be drawn.

#### 4.3.1.4 Molecular Basis of Infection

##### Pro-inflammatory Cytokines

Chemokines (IL-8), the pro-inflammatory cytokines (IL-1 $\alpha$ , TNF- $\alpha$ ), and other mediators (e.g., platelet-activating factor, prostaglandins) are central to infection-induced PTL. IL-1 is implicated in the onset of infection-induced PTL: (1) IL-1 is produced by human decidua in response to bacterial products; (2) IL-1 $\alpha$  and IL-1 $\beta$  stimulate prostaglandin production by human amnion and decidua; (3) IL-1 $\alpha$  and IL-1 $\beta$  concentrations and IL-1-like bioactivity are increased in the amniotic fluid of women with PTL and infection; (4) intravenous IL-1 $\alpha$  stimulates uterine contractions; and (5) administration of IL-1 to pregnant animals induces PTL, and this effect can be blocked by the administra-

tion of its natural antagonist, the IL-1 receptor antagonist (IL-1ra).

The role of TNF- $\alpha$  in the mechanisms of PTL is similar: (1) TNF- $\alpha$  stimulates prostaglandin production by the amnion, decidua, and myometrium; (2) human decidua can produce TNF- $\alpha$  in response to bacterial products; (3) amniotic fluid TNF- $\alpha$  bioactivity and immunoreactive concentrations are elevated in women with PTL and IAI; (4) in women with PPROM and IAI, TNF- $\alpha$  concentrations are higher in the presence of labor; (5) TNF- $\alpha$  can stimulate the production of MMPs, implicated in membrane rupture; (6) TNF- $\alpha$  application to the cervix induces changes that resemble cervical ripening; (7) TNF- $\alpha$  can induce PTL by inducing apoptosis via the Fas ligand and stimulates the production of uterotonic agents such as endothelin [88]; and (8) TNF- $\alpha$  and IL-1 $\alpha$  enhance IL-8 expression by decidual cells, and this chemokine is strongly expressed by term decidual cells in the presence of chorioamnionitis. Other cytokines and chemokines (IL-6, IL-16, IL-18, colony-stimulating factors, macrophage migration inhibitory factor, monocyte chemoattractant protein-1, epithelial cell-derived neutrophil-activating peptide, etc.) are implicated in the complex host response to pathogenic insults and infection-induced PTL. The redundancy of the cytokine network implicated in parturition is such that the blockade of a single cytokine is insufficient to prevent infection-induced PTL. However, blockade of both IL-1 and TNF- $\alpha$  signaling pathways in mice was associated with a decreased rate of PTL, partly because IL-1 and TNF mediate some of their effects via COX-2 [89]. Even the combined inhibition of IL-1 and TNF- $\alpha$  does not entirely abolish susceptibility to bacterially induced labor, suggesting that there are yet other important factors.

Prostaglandins produced in the amnion are inactivated by prostaglandin dehydrogenase released by the chorionic tissue. This prevents prostaglandins from reaching the myometrium to cause uterine contractions [73]. Infection of the chorion inhibits the activity of prostaglandin dehydrogenase, thereby allowing prostaglandins to reach the myometrium and cause premature contractions [90].



Anti-Inflammatory Cytokines

IL-10 is a crucial cytokine for the maintenance of pregnancy. With IAI, concentration increases, suggesting that IL-10 dampens the inflammatory response and may have therapeutic value. In a nonhuman primate model of IAI, dexamethasone and IL-10 treatment significantly reduced IL-1 $\alpha$ -induced uterine contractility. The amniotic fluid concentrations of TNF- $\alpha$  and leukocyte counts were also decreased by IL-10 treatment. Furthermore, the administration of IL-10 in animal infection models has been associated with improved pregnancy outcomes.

Cytokeratins

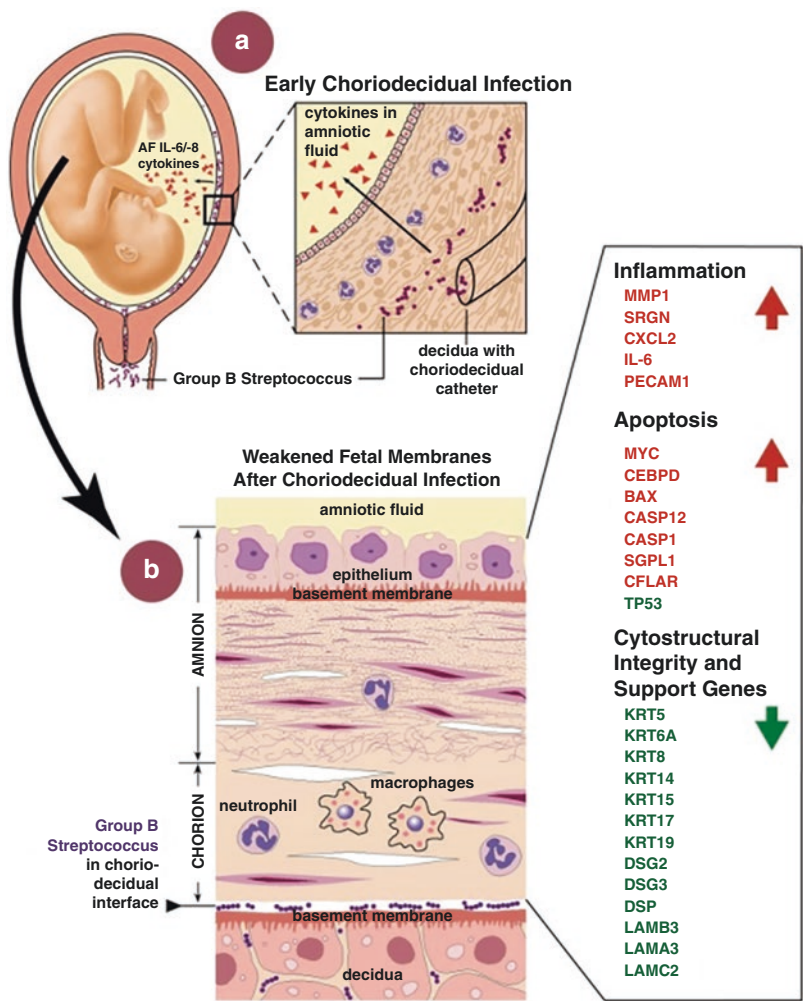
The early choriodecidual infection decreases cellular membrane integrity and tensile strength via

dysfunction of cytokeratin networks. Downregulation of cytokeratin expression and perturbations in the amniotic epithelial cell intermediate filament network occur after Group B Streptococcus choriodecidual infection, which may contribute to PPROM (Fig. 4.4).

4.3.2 Maternal and Fetal Stress

The bombardment of Strassbourg in 1870 produced many abortions, probably through fright. A similar observation was by Bouvocque with 92 uninjured women after a powder mill exploded in Grenelle. On the contrary, the bombing of Hiroshima did not affect the interruption of pregnancy. Moreover, abortions were no greater in

**Fig. 4.4** The pathway of ascending intrauterine infection. (Reproduced with permission from [91] under the CC BY 4.0)

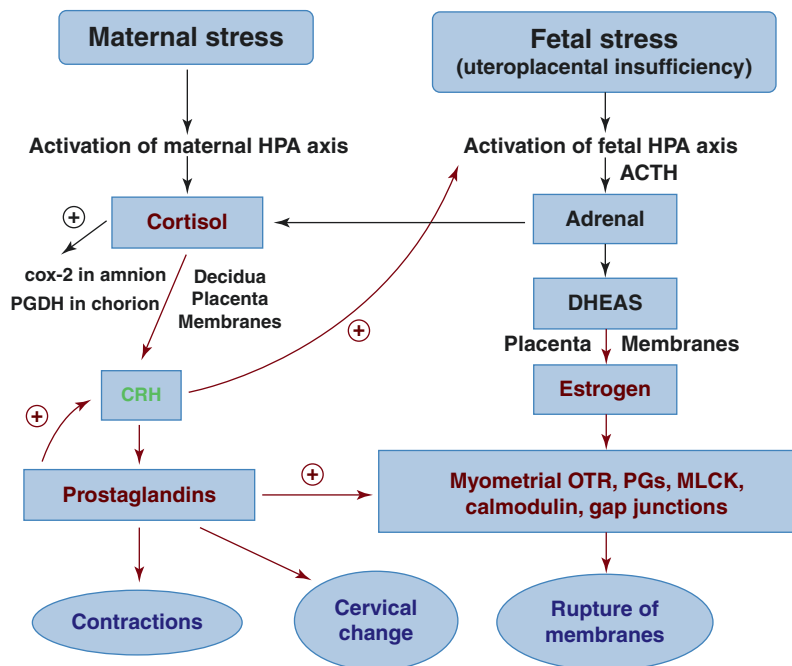


London than before the bombings of World War II. Increased intra-abdominal pressure (see Chap. 3) could be an important etiologic factor in explosions rather than emotional disturbance [92].

The maternal stress of exogenous or endogenous origin is modestly associated with an increased risk for PTL. The stressful insult could occur in the pre-conceptional period or during pregnancy. The precise mechanism is unknown; however, it includes a CRH. The hormone was originally identified in the hypothalamus, but is expressed by the placenta. The maternal plasma CRH concentrations increase during the second half of pregnancy and peak during labor, whereas serum concentrations of the CRH-binding protein decline during the third trimester. The trajectory of CRH serum concentration changes identifies women destined for preterm, term, and post-term delivery. The mechanisms regulating the serum concentration and trajectory of CRH have been described as “a placental clock”. The mechanisms through which CRH activates the common pathway of parturition include: (1) increased production of PGE<sub>2</sub> by the amnion, chorion, and placental cells, but not by decidual cells; (2) increased production of PGF<sub>2</sub>α by the

amnion, decidua, and placental cells, but not by chorion; (3) increased expression of MMP-9 by chorion and amnion; (4) stimulation of the release of adrenocorticotropin (ACTH) from the pituitary gland to drive fetal cortisol production (this establishes a feed-forward cycle because cortisol stimulates the production of CRH by the placenta and fetal membranes); (5) induction of the synthesis of fetal DHEAS by the fetal adrenal zone (the human placenta lacks the enzyme 17-hydroxylase, and it is not able to convert progesterone to estrogen as occurs in other mammals [93]. Fetal DHEAS is the primary substrate converted by the placenta to estrogen, which in turn enhances the expression of the oxytocin receptor, COX-2, prostaglandin receptors, and connexin-43); (6) cortisol in response to CRH can increase amnion COX-2 expression while inhibiting chorionic PGDH expression (resulting in a net bioavailability of prostaglandins); and (7) CRH inhibits progesterone production by the placenta. Figure 4.5 illustrates the molecular mechanisms for stress-associated PTL. As noted, CRH has been implicated in the mechanisms of spontaneous parturition at term. Therefore, this specific pathway may operate in normal term labor

**Fig. 4.5** Proposed pathways by which stress can induce preterm labor. *ACTH* adrenocorticotrophic hormone, *CRH* corticotropin-releasing hormone, *DHEAS* dehydroepiandrosterone sulfate, *HPA* hypothalamic-pituitary-adrenal, *PG* prostaglandin, *COX-2* cyclo-oxygenase 2, *PGDH* 15-hydroxyprostaglandin dehydrogenase. (Reproduced with permission from [94])





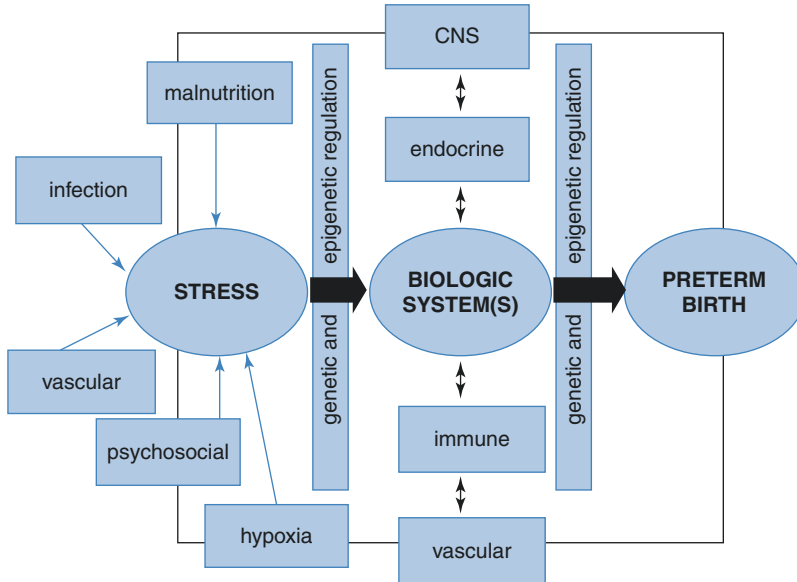
and PTL. In the former case, placental CRH expression reflects the maturation of the fetal hypothalamic-pituitary-adrenal axis; in the latter, it reflects physiologically stressful events occurring at later gestational ages. It may be surmised that some cases of PTL occurring close to term resort to the physiologic mechanisms used in term labor after stressful stimuli have accelerated fetal maturation.

Although the concept that psychosocial stress may contribute to PTL risk through its effects on several stress-sensitive biologic processes implicated in parturition, tests of pathway (meditational) models did not confirm a causal relationship. Cortisol production in vivo is influenced not only by the psychological state of the individual, but also concurrently by a host of other conditions, such as variations in the nutritional milieu, physical activity, infection/inflammation, hypoxia, sleep, chronobiological state, and, in the case of pregnancy, by the stage of gestation. Moreover, the effects of psychological

stress on cortisol production likely vary due to other conditions (i.e., an interactional, conditional, or effect-modification model). Second, it is unknown when perturbation within a particular biologic system remains constrained within that system. Adopting and implementing a systems biology approach will be required to uncover the complex interrelationships and pathways inherent in vivo human models of complex multifactorial disorders such as PTL (Fig. 4.6).

### 4.3.3 Decidual Hemorrhage

Decidual hemorrhage (placental abruption) originates in damaged spiral arteries or arterioles and presents clinically as vaginal bleeding, or retroplacental or retrochorionic hematoma formation noted on ultrasound (US). Decidual hemorrhage secondary to placental abruption is histologically noted in up to 60% of PTB [96]. The association of abruption with increasing maternal age may



**Fig. 4.6** Contribution of maternal stress and stress biology to preterm birth. No one-to-one correspondence exists between psychosocial stress and stress-sensitive biology; the nature, magnitude, and duration of the effects of maternal psychosocial stress during pregnancy on any given stress-sensitive biologic system are altered by the context of other conditions/stressors, including nutrition,

infection, and hypoxia. Similarly, the nature, magnitude, and duration of the effects of a given stress-sensitive biologic system in pregnancy on maternal and fetal target systems involved in parturition are altered by the secondary perturbations in other closely related biologic systems and their feedback effects. (Reproduced with permission from [95])

reflect an increase in myometrial artery sclerosis, which increases from 11% of spiral arteries at age 17–19 years to 83% after age 39 [97].

Three principal mechanisms for the initiation of placental abruption are:

- Decidual spiral arteries disruption,
- Infection-induced placental abruption,
- Trauma-induced placental abruption.

#### 4.3.3.1 Decidual Spiral Arteries Disruption

The decidua is a rich source of tissue factor, the primary initiator of clotting through thrombin generation [98]. Following the spiral arterial vascular disruption, the decidual tissue factor is exposed to and can complex with plasma factor VII to generate factor Xa that, in turn, converts prothrombin to thrombin. Thrombin subserves some hemostatic functions to produce a retroplacental or retromembranous thrombus. However, in addition to its procoagulant properties, thrombin also enhances the expression of tissue-type and urokinase-type plasminogen activators (uPA and tPA), which directly degrade fibronectin and generate plasmin from plasminogen which degrades laminin, collagen III, and fibronectin, crucial components of the decidua and fetal membranes [99].

MMP-1 and MMP-3 protein expression is enhanced by thrombin binding to its receptor, protease-activated receptor type-1 (PAR-1) [100, 101]. Thrombin also enhances MMP-9 expression [102]. Abruption-associated PPRM is accompanied by dense decidual neutrophil infiltration without infection [103]. Neutrophils are a rich source of elastase and MMP-9 [104], contributing to PPRM and cervical effacement. These findings suggest that a mechanism linking abruption-associated PPRM to decidual thrombin–PAR interactions triggers myometrial contractions [105].

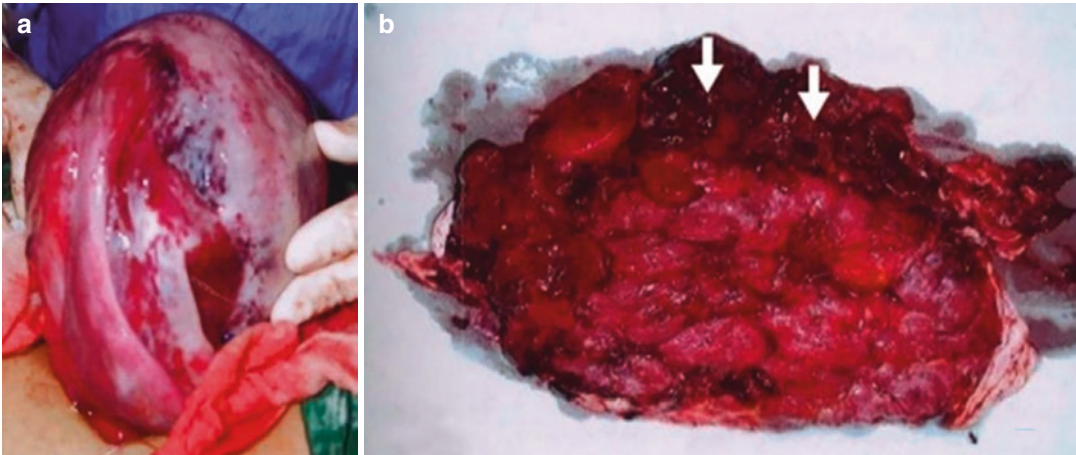
#### 4.3.3.2 Infection-induced Placental Abruption

In all abruptions, the proportion of intrauterine infections is 6.7% and is threefold higher than

without intrauterine infection [106]. Histologically confirmed chorioamnionitis is 30% among women with placental abruption [107] and is strongly associated with placental abruption in both term and preterm pregnancies [107]. With maternal intraperitoneal infection, microorganisms may access the intervillous space by hematogenous dissemination during maternal bacteremia. From there, the infection could spread to the villi and fetal circulation. Histologic chorioamnionitis and funisitis are significantly more common with acute, severe preterm placental abruption than in normal deliveries [108]. Another route could be the retrograde transport of bacteria through the Fallopian tubes, causing chorioamnionitis. Direct bacterial colonization of the decidua in generalized peritonitis with resultant tissue inflammation may initiate disruption of decidual lysosomes and tissue disruption, which results in placental abruption [109].

Placental abruption or uteroplacental apoplexy (Couvelaire uterus) induced by acute pancreatitis is rare, mostly during the third trimester [110, 111]. Placental abruption likely occurs in the first phase of AP, resulting from a systemic inflammatory response (Fig. 4.7). Studies in animal models found markedly increased expression of E-selectin in serum and placenta tissues 1 h after induction of pancreatitis. The concentration of E-selectin was significantly related to the degree of pancreatic and placenta injury [112]. Another mechanism of placental injury during pancreatitis might be associated with activating the mitogen-activated protein kinases pathway, particularly c-Jun N-terminal kinase and p-38 [113].

Placental abruption is several-fold higher in patients with acute appendicitis [114]. Placental abruption after acute appendicitis occurs during the third trimester [108, 115–117]. The association between the severity of acute appendicitis or type of bacteria and placental abruption is unknown because, in a single case, the bacteria was described (*E. coli*), and culture specimens from the neonate's nose, pharynx, and ear canals were sterile [108].



**Fig. 4.7** (a) Uteroplacental apoplexy means extravasation of blood into the uterus myometrium, and serosa. (b) Blood clots adherent to the placenta (arrows) indicates

abruptio placentae caused by uteroplacental apoplexy. (Reproduced with permission from [111])

#### 4.3.3.3 Trauma-induced Preterm Labor

##### Placental Abruptio

See Sect. 25.3.6.1.

##### Traumatic Uterine Contractions

Uterine contractions induced by uterine trauma are the result of two processes. First is when a traumatic uterine injury destabilizes lysosomal enzymes that can initiate prostaglandin production. Second, thrombin produced by actively clotting blood interacts with the *protease-activated receptors* in the myometrium, resulting in robust uterus contractions, even without prostaglandin production [118]. Thrombin at concentrations 1–100 U/mL represents less thrombin generated by 1 mL of clotting blood and stimulates myometrial contractions in a dose-dependent fashion. Thrombin activates the phosphatidylinositol signaling pathway and generates cytosolic calcium oscillations [119].

Maternal demographic factors, presence of uterine contractions, maternal clinical conditions (abdominal pain, abdominal tenderness, vaginal bleeding), hematologic and coagulation studies, US findings, fetal heart rate tracing category, AIS score for abdomen, and ISS score do not predict preterm delivery or other secondary outcomes [120].

#### 4.3.4 Maternal Nutritional Status

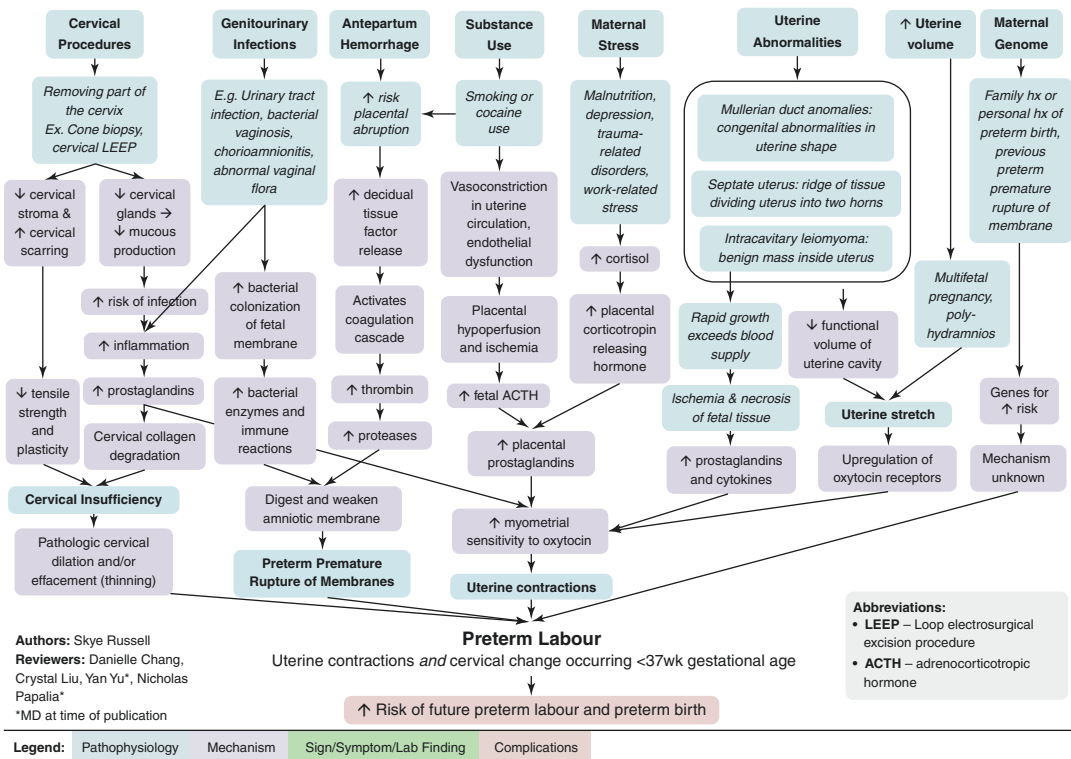
Many causes of fetal morbidity, in addition to PTL, are due to the loss of adequate maternal nutrition during pregnancy. A low prepregnancy BMI is associated with a high risk of spontaneous PTB, whereas obesity can be protective [121]. Women with low serum iron, folate, or zinc have more PTB [122, 123]. Maternal thinness is associated with decreased blood volume and reduced uterine blood flow, increasing the rate of PTL [124].

The acute abdomen during pregnancy results in three scenarios of prolonged maternal starvation as follows:

- recurrent or persistent symptomatology of underlying disease such as symptomatic cholelithiasis/cholecystitis, acute/chronic pancreatitis, adnexal torsion, etc.,
- postoperative catabolism with inadequate IV supplementation,
- protracted posttreatment sepsis/septic shock.

Peroral nutrition is inadequate mainly due to a higher basal metabolism in systemic inflammation leading to body mass loss in all these scenarios. Due to blood redistribution in sepsis, uterine blood flow can further be decreased.

### Preterm Labour: Pathogenesis & Maternal Complications



**Fig. 4.8** Pathogenesis of preterm delivery. (Reproduced with permission from [129])

#### 4.3.5 Final Common Pathway

The generation of prostaglandins and proteases reflects the final common delivery pathway, preterm or at term. Prostaglandin levels increase in reproductive tract tissues, maternal plasma, and amniotic fluid immediately before and during parturition [125, 126]. Concurrent with rising prostaglandin levels is the upregulation of myometrial prostaglandin receptors before labor onset [127, 128]. Prostaglandins induce functional progesterone withdrawal, enhance sensitivity to estrogens, and increase MMP and IL-8 expression. Moreover, all the pathways of prematurity described above also directly trigger MMP and IL-8 expression to mediate cervical change and fetal membrane rupture. The myometrium is quiescent before 20 weeks' gestation because of the high PR-B, low ER- $\alpha$ , low circulating estrogen levels, and inhibition of CAP gene expression. Therefore,

inflammation, abruption, and excess stretch occurring before 24 weeks present as “incompetent cervix” with or without subsequent PPROM and not PTL. Figure 4.8 presents the discrete pathogenic processes leading to prematurity and their final common biochemical pathway.

#### 4.4 Clinical Presentation

Clinical presentation of acute abdomen warrants a search of its cause and other potential causes of PTL. For pregnant patients with abdominal trauma, maternal hemodynamic status should be checked first (see Chap. 25), then the cause of acute abdomen and PTL should be evaluated. Sometimes a clinical picture is challenging to establish due to attenuated inflammatory response. Several authors observed this in the late nineteenth century [130].

One-third of all patients with PTL have intact membranes, one-third present with PPROM, and one-third result from indicated delivery (delivery in response to maternal or fetal complications) [131].

Diagnosis of ROM is made by sterile vaginal examination by speculum in women presenting with a suspicious clinical history or US detected oligohydramnios. Confirmation of vaginal lacerations or bony fragments may indicate pelvic fractures. Evident fluid passing through the cervical os is diagnostic.

For the presentation of traumatic placental abruption, see Sect. 25.3.6.1.

## 4.5 Diagnosis

### 4.5.1 Prediction of Preterm Labor

#### 4.5.1.1 Uterine Contractions

Intrauterine infection is associated with uterine contraction frequency or PTL [132–134]. However, uterine contractions do not predict PTL well in singletons because of the wide variation in frequency in normal pregnancy and PTL [134]. Similar results were found in twins [135]; however, women admitted with a diagnosis of PTL, if they do not deliver, remain at increased risk of subsequent PTL and PPROM.

#### 4.5.1.2 Laboratory Findings

A marked correlation of elevated CRP and ALP in women with non-acute abdomen PTL was observed compared to women without PTL, whereas the best cut-off values of CRP >20–27 mg/L and ALP >300–399 IU/L were the best values in the prediction of PTL [136, 137]. Currently, no studies predict PTL in pregnant patients with acute abdomen.

Most patients with acute abdomen have elevated CRP values and are at increased risk for PTL.

### 4.5.1.3 Transvaginal Ultrasound

Transvaginal US has shown that a short cervix (cervical length  $\leq 25$  mm) is associated with IAI and an increased risk of adverse pregnancy outcomes [83, 138]. Women with a cervical length of  $\leq 15$  mm between 22 and 30 weeks of gestation have a higher rate of microbial invasion of the amniotic cavity and are more likely to deliver spontaneously before 35 weeks of gestation [139]. Therefore, the US cervical length may be a valuable predictor of the risk of microbial invasion of the amniotic cavity and IAI [83]. Unfortunately, there are no studies in patients with localized/diffuse peritonitis or abdominal trauma when PTL develops quickly, in hours or days.

### 4.5.2 Preterm Premature Rupture of Membranes

The presence of vaginal bleeding outside the first trimester has been associated with a sevenfold increase in the risk of PROM and a 2.9-fold increased risk of PTB [96].

An alkaline vaginal pH (6.0–6.5) and a “ferning” pattern on microscopic examination of dried vaginal secretions are supportive (normal vaginal secretions have a pH of 5.0, whereas amniotic fluid has a pH of 7.0) when visual inspection is equivocal. False-positive findings are due to cervical mucus, blood, semen, alkaline antiseptics, or bacterial vaginosis. False-negative results are from prolonged leakage and oligohydramnios. Repeat speculum examination after prolonged bed rest may provide diagnostic information if initial testing is negative despite a suspicious history. In the absence of fetal growth restriction or urogenital abnormalities, US evidence of oligohydramnios is suggestive but not diagnostic of ROM. The diagnosis can be confirmed by indigo carmine amnioinfusion with the transvaginal passage of dye. A search for concomitant maternal and fetal injuries is mandatory, and prolonged continuous fetal monitoring is advocated.

### 4.5.3 Placental Pathology

Placental pathology has a better predictive value for IAI than clinical signs and symptoms. Placental histology has a high negative predictive value (97%) and reasonable positive predictive value (79%) for diagnosing IAI compared with fluid cultures [140]. Placental pathology has a twofold improvement in positive predictive value compared with the clinical signs and symptoms of IAI [141]. Unfortunately, placental pathology can be obtained when the patients' management has been completed without influencing the immediate therapeutic process.

## 4.6 Treatment

With extrauterine intra-abdominal infection, the underlying cause and the PTL should be treated simultaneously. With maternal abdominal trauma, the mother should be stabilized first (see Chap. 25), then PTL treated.

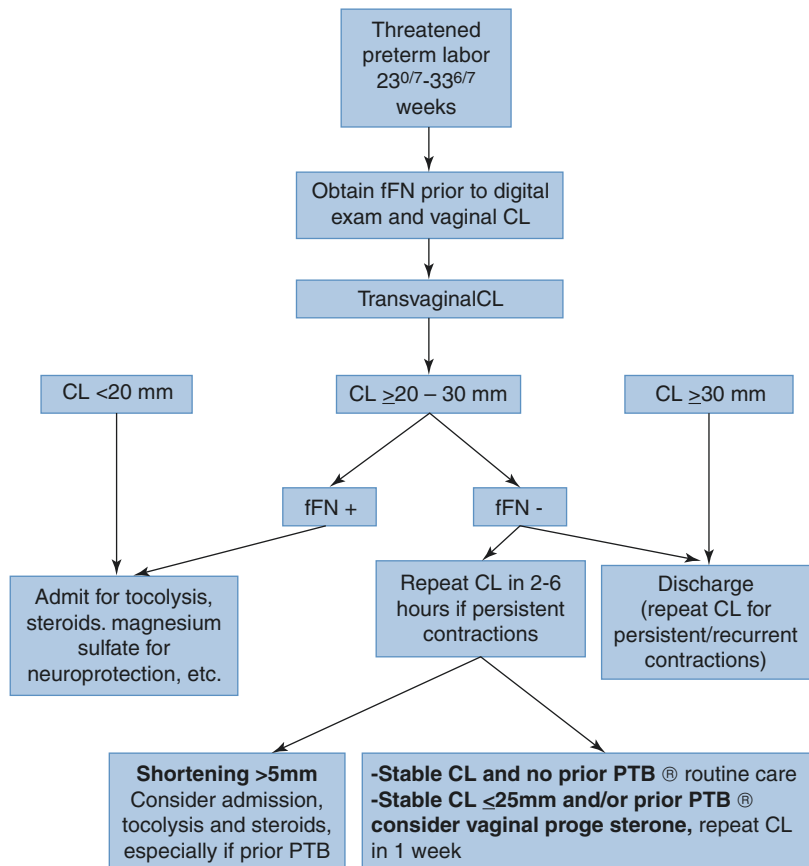
The vast majority (70–80%) of the women with symptoms of all-cause spontaneous PTL do not deliver preterm even without intervention. The most common criteria for PTL are uterine contractions ( $\geq 4/20$  min or  $\geq 8/h$ ) and cervical change with intact membranes at 20–36 weeks 6 days.

Women without cervical change do not have PTL and should not receive tocolysis. Women with PTL but negative fFN and TVU CL  $\geq 30$  mm have a less than 1% chance of delivering within 1 week and a more than 95% chance of delivering  $\geq 35$  weeks without therapy [142] and should not receive tocolysis.

The complete diagnostic-therapeutic algorithm is presented in Fig. 4.9.

In infection-induced PTL prevention, therapeutics should ideally eliminate the microorgan-

**Fig. 4.9** Suggested algorithm for evaluating and managing threatened preterm labor. (–) negative, (+) positive, CL cervical length, fFN fetal fibronectin, PTB preterm birth. (Reproduced with permission from [143])





isms from the amniotic cavity and block the ensuing cytokine cascade that drives the release of PGs and matrix metalloproteinases (MMPs), prevent the onset of PTL, and minimize the risk of FIRS.

Thirty-four weeks of gestation is a threshold at which perinatal morbidity and mortality are too low to justify the potential maternal and fetal complications and costs associated with the inhibition of labor and short-term delivery delay [144, 145]. Tocolytics are not indicated before viability (23–24 weeks of gestation) since these drugs do not delay delivery for more than a few days [146].

One explanation for the inefficient longer delay of PTB is that most interventions are directed on only one of many perplexing pathways of the complex process of parturition (see Sect. 4.2).

#### 4.6.1 Nontocolytic Treatment

##### 4.6.1.1 Bed Rest

Bed rest has never been tested in singleton gestations complicated by PTL or PPROM. In twin pregnancies with cervical dilatation, bed rest in the hospital has not been shown to decrease PTL [147].

##### 4.6.1.2 Antibiotics

The lack of antibiotic effectiveness in all-cause PTB may be the result of (1) a therapeutic application long after the infection is established [148], (2) the difficulties in identifying the specific pathogens and prescription of the pathogen-specific therapy, (3) an increase in PTB in some subgroups [149], and 4) potential adverse effects on neonatal outcomes.

##### Intrauterine Infection

Antibiotics are given to women with intrauterine infection-induced PTL. However, it is not the infection but the subsequent inflammation that

initiates PTL and is primarily responsible for adverse neonatal outcomes. An exception is an improvement in women with PPROM with antibiotics such as erythromycin. These results include increased latency before labor and improved neonatal outcomes [150, 151].

Compared with metronidazole, clindamycin has similar activity against anaerobes. However, it is far superior concerning broad-spectrum activity, group B streptococcus (associated with PTL when present as heavy colonization), and many other bacterial vaginosis-related organisms, particularly fastidious organisms such as *M. hominis* [152, 153]. Also, clindamycin has anti-inflammatory properties [154, 155]. There is merit in oral and intravaginal administration of clindamycin to eradicate abnormal genital tract flora/bacterial vaginosis in pregnancy. Vaginal administration delivers the highest concentration of antibiotics to the site of the heaviest bacterial load. On the other hand, bacterial vaginosis could be associated with subclinical endometritis [156], so if vaginal organisms have already gained access to the choriodecidea, these organisms may not be accessible to vaginal administration. Therefore, systemic therapy may provide benefits. There are no studies on the combined use of oral and vaginal clindamycin. Even if this reverts to normal, abnormal genital tract flora in early pregnancy is still associated with LM and PTB. This suggests that whatever damage is done by infection/inflammation occurs early and persists [157]. Suppose antibiotics are used late in pregnancy when inflammatory tissue damage may have already occurred, with irreversible changes in the cervix, myometrium, decidua, placenta, and extra-placental membranes. In that case, antibiotics are unlikely to be beneficial [158, 159]. Unfortunately, some of these studies were not adequate.

The immune system is primed *in utero* and modified after birth. Accordingly, antibiotics during pregnancy or the neonatal period may disrupt the developing neonatal gut microbiome, failing immune response maturation, resulting in asthma, allergy, and atopic disease [160–163]. This has led to new diets and gut microflora treatments for newborns.



### Acute Abdomen

Studies on antibiotic prevention of infection-induced PTL did not include pregnant patients with extrauterine intra-abdominal infection (IAI). The general recommendations are:

- removal of the infective source with dosage and duration of antibiotic therapy as indicated by guidelines for the treatment of the primary infective cause, not for the prevention of uterine contractions and PTL,
- IV clindamycin, in addition to other antibiotics indicated for patients with acute abdomen or abdominal trauma with unknown group B *Streptococcus* culture status (especially before 32 weeks of pregnancy), should be administered.

Abdominal trauma patients are a specific subgroup because infection-induced PTL is not the primary mechanism. Antibiotic treatment of all women with threatened PTL to prevent neonatal infection with group B streptococcus is recommended because preterm infants have an increased risk of this infection [164]. Rates of neonatal group B streptococcus infection and corresponding mortality rates have declined since this strategy was adopted in the USA [164]. Preterm infants with traumatic injuries and possible hemodynamic instability (due to maternal hemorrhagic shock) or blood loss are particularly susceptible to neonatal infections.

#### 4.6.1.3 Antioxidants

In vitro studies indicate that vitamins C and E can prevent tissue damage to chorioamniotic membranes inflicted by hypochlorous acid, a reactive oxygen species produced by host cells during infection and inflammation [165]. Although the dose-response relationship between the plasma ascorbic acid concentration and the prevalence of PPROM has been shown,

ascorbic acid concentrations may have only reflected the general nutritional status of patients [166]. The issue is that studies focused on single, for example, hypochlorous acid-induced damage [165], whereas *in vivo* infection-induced damage could occur via nonoxidative pathways (e.g., elastase, protease). The diet alone could be an inadequate source of vitamins C and E during pregnancy, and supplementation may reduce PPROM [167]. Supplemental intake of vitamins C and E to prevent preeclampsia did not lower PTB and PPROM rates, but respiratory morbidity was reduced [168]. The role of antioxidants in preventing PTL in acute settings (i.e., peritonitis/intra-abdominal trauma) is unknown.

#### 4.6.1.4 Inhibitors of Thrombin-mediated Contractions

Uterine trauma can cause nonplacental abruption uterine bleeding that activates thrombin. Thrombin causes uterine contractions even without prostaglandin synthesis (see Sect. 4.3.3.3). IV hirudin, a direct thrombin inhibitor, was used for other emergent indications in pregnancy and should be evaluated for this indication [169]. Another consideration is whether to administer r-hirudin as prophylactic therapy or only when uterine contractions are present and other causes for uterine contractions are excluded. The oral direct thrombin inhibitor, ximelagatran, was withdrawn due to potential hepatotoxicity [170]. This therapy could be contraindicated in trauma-induced uterine bleeding.

Thrombin-stimulated myometrial contractions could be suppressed with inhibitors of the phosphatidylinositol signaling pathway [171].

#### 4.6.1.5 Vitamin D

Maternal circulating 25-OHD deficiency could increase overall PTL risk, and vitamin D supplementation alone during pregnancy could reduce PTB risk. The effect was significant with maternal serum 25-OHD <50 nmol/L [172]. Although not analyzed for pregnant patients with acute abdomen, vitamin D supplementation in the perioperative period could decrease the likelihood of PTL.

### 4.6.2 Tocolytic Treatment

Seventy years ago, it was stated that, when peritonitis is present, CS is mandatory [173–175], and cesarean hysterectomy in more severe cases of abscess formation may prove lifesaving. Although preterm contractions caused by uterine irritation from peritonitis occur in up to 83% of the cases, PTL and delivery occur in only 5–14%. However, >50% of these patients in the third trimester deliver preterm [176]. *True* PTL can be defined as uterine contractions with transvaginal CL <20 mm, or CL 20–29 mm with a positive fetal fFN [177]. *Threatened* PTL is when a woman has symptoms of PTL, such as contractions or cramping, but no cervical change, for example, a transvaginal CL  $\geq$ 30 mm.

Women with true PTL should receive tocolysis and corticosteroids. Despite symptoms, there is no need for therapy in threatened PTL, including tocolysis [177].

For patients with true PTL, tocolytic therapy can temporarily abolish contractions. However, it does not remove the underlying stimulus that initiated the process of parturition or reverse parturition changes in the uterus and cervix. Prematurity is associated with adverse neonatal outcomes, while tocolytic agents can cause adverse neonatal effects. Between 23 and 26 completed weeks of gestation, each day of prolongation of pregnancy increases the survival rate by 3% [178].

Prostaglandin inhibitors and calcium channel blockers are the tocolytics with the best probability of 48 h delay in all-cause PTL, respiratory distress syndrome, neonatal mortality, and maternal side effects [179].

The probability of postponed delivery for 48 was highest with prostaglandin inhibitors (OR

5.39), followed by magnesium sulfate (OR 2.76), calcium channel blockers (OR 2.71), betamimetics (OR 2.41), and the oxytocin receptor blocker atosiban (OR 2.02) [179].

Tocolytic treatment after the onset of contractions could not prevent PTL and should be ordered for patients with delayed presentation and advanced gestational age to prevent PTL and fetal loss [180]. Tocolysis only delays PTD for several days, but PTD is not prevented [181].

No study has documented positive effects on the outcome. The current recommendation is that using these agents is a matter of choice [182–184].

SAGES and EAES guidelines recommend tocolytics only if uterine contractions are present.

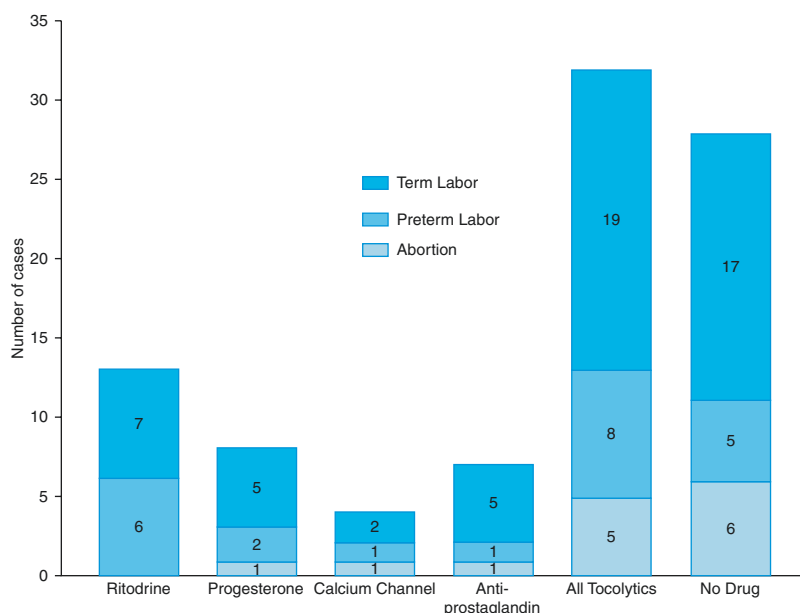
Tocolytics could calm the uterus from the insult of the acute abdomen and the intraoperative uterine manipulation, but their benefit is equivocal [185, 186]. There is no significant difference in the efficacy of different tocolytics or outcomes with or without tocolytics (Fig. 4.10) [187]. Also, tocolytics have severe maternal and fetal side effects, which could contraindicate their use, especially ritodrine and prostaglandin synthetase inhibitors.

Ritodrine causes maternal and fetal tachycardia, nausea, and vomiting [188, 189], impairing important signs of the acute abdomen. Unlike ritodrine and prostaglandin synthetase inhibitors, nifedipine is safer and does not alter the disease symptomatology [185]. Nifedipine causes insignificant hypotension [189, 190]. The evidence for teratogenicity [191] is not conclusive [192], and no malformations were reported [188].

Nearly 26% with symptomatic cholelithiasis developed preterm contractions requiring tocolysis [193]. Tocolysis is used only if uterine contractions are present [194].

*Maintenance Tocolysis:* While acute tocolysis delays delivery of >48 h and enables completion of antenatal corticosteroid administration and

**Fig. 4.10** No statistically significant difference between different tocolytics with their effect on the duration of pregnancy and prevention of preterm labor in the acute abdomen. (Reproduced with permission from [188])



patient's transfer to a tertiary perinatal center, maintenance tocolysis is still controversial. So far, maintenance of tocolysis is a case-by-case decision outweighing its benefits and harms (Table 4.1).

#### 4.6.2.1 Magnesium Sulfate

Magnesium is not metabolized, and elimination of the drug is conducted mainly through renal excretion. Therefore, the difference in clearance during and after pregnancy likely reflects modifications in renal clearance. Pregnant women receiving magnesium sulfate for non-preeclamptic indications (i.e., neuroprotection and tocolysis) have an increased clearance of the drug compared with preeclamptic women [196].

#### Abdominal Trauma

Maternal trauma can cause PPRM and PTB, but is seldom an isolated event. At <24 weeks of gestation, ROM may predispose the fetus to pulmonary hypoplasia or orthopedic deformities if the amniotic fluid volume does not return to normal. With the injury to the placenta, bleeding may result in fetal anemia, hypovolemia, or both. Management is usually not different from spontaneous ROM in the absence of maternal or fetal compromise.

The use of tocolysis to treat PTL after blunt abdominal trauma is limited. Tocolysis is not recommended because regular uterine activity after a traumatic event could result from a uterine contusion or placental abruption and these two diagnoses are indistinguishable [197]. There are cases of placental abruption with <1 uterine contraction every 10 min. In that population, almost 20% with frequent contractions had placental abruption [197]. In noncatastrophic abdominal trauma in pregnancy, tocolysis for persistent contractions is reassuring after the maternal and fetal testing results [198].

Magnesium sulfate is the tocolytic agent of choice for pregnant patients with abdominal trauma, with the added effect of fetal neuroprotection to decrease the risk of cerebral palsy. Minimal dose includes 4 g loading dose + 1 g/h maintenance dose over 12 h.

The PTL group received more magnesium sulfate tocolysis than the term birth group (31% vs. 7%, respectively). However, there were no differences in the gestational age at abdominal

**Table 4.1** Classes and substances for maintenance tocolysis

| Substance class               | Administration route          | Substance                                                 | PTB rate- reduction | Improvement of neonatal outcome | Side effect risk | Recommendation        |
|-------------------------------|-------------------------------|-----------------------------------------------------------|---------------------|---------------------------------|------------------|-----------------------|
| Beta-sympathomimetics         | Oral, parenteral: bolus, pump | Terbutaline, fenoterol, ritodrine                         | No                  | No                              | High             | Not recommended       |
| Calcium-channel blockers      | Oral                          | Nifedipine                                                | No                  | No                              | Intermediate     | Case-by-case decision |
| Cyclooxygenase inhibitors     | Oral/rectal/vaginal           | Indomethacin                                              | No                  | No                              | Intermediate     | Case-by-case decision |
| Magnesium                     | Oral/parenteral               | Magnesium sulfate                                         | No                  | No                              | Intermediate     | Not recommended       |
| Nitric oxide donors           | Transdermal                   | Nitroglycerine                                            | No                  | No                              | Intermediate     | Not recommended       |
| Oxytocin receptor antagonists | Parenteral                    | Atosiban                                                  | No                  | No                              | Low              | Not recommended       |
| Progesterone                  | Oral/vaginal intramuscular    | Micronized progesterone, 17α-hydroxyprogesterone caproate | No                  | No                              | Low              | Not recommended       |

Reproduced with permission from [195]

trauma and the interval between trauma and delivery between groups. In abdominal trauma, patients with PTB had a closed and no effaced cervix at the time of abdominal trauma [198]. Magnesium sulfate in non-acute abdomen PTL is neuroprotective. It improves long-term neonatal health outcomes, despite maternal side effects (decreases respiratory efforts and, in high doses, may lead to hypotension, respiratory collapse, or cardiac arrhythmias). While magnesium sulfate has not significantly improved cognition and behavior outcomes at school age, it prevents cerebral palsy at 2 years [199]. The most beneficial dosing regimen for neuroprotection remains unknown [196]. Magnesium readily crosses the placenta, with an almost 1:1 ratio of magnesium in the pregnant mother and umbilical cord [200]. Magnesium levels increase in fetal serum within 1 h and amniotic fluid within 3 h after maternal IV administration [200]. Among pregnant women with preeclampsia, serum magnesium levels were significantly greater during magnesium sulfate infusion than non-preeclamptic women receiving the same magnesium sulfate dosing. Women with the greatest body weight had lower serum magnesium levels after the bolus administration of magnesium sulfate than women with the lowest body weight (Fig. 4.11).

Several classes of tocolytic agents are not recommended in abdominal trauma. Betamimetics ( $\beta_2$ -adrenergic agonists) cause maternal and fetal

tachycardia. They can mask the clinical signs of hypovolemia in both the mother and the fetus, leading to a delay in the institution of the appropriate intervention. NSAIDs/Indomethacin affect platelet function and are contraindicated in patients with head injury or occult bleeding. Calcium channel blockers may produce hypotension. Such vital sign changes mimic those seen in occult hemorrhage, mandating close monitoring.

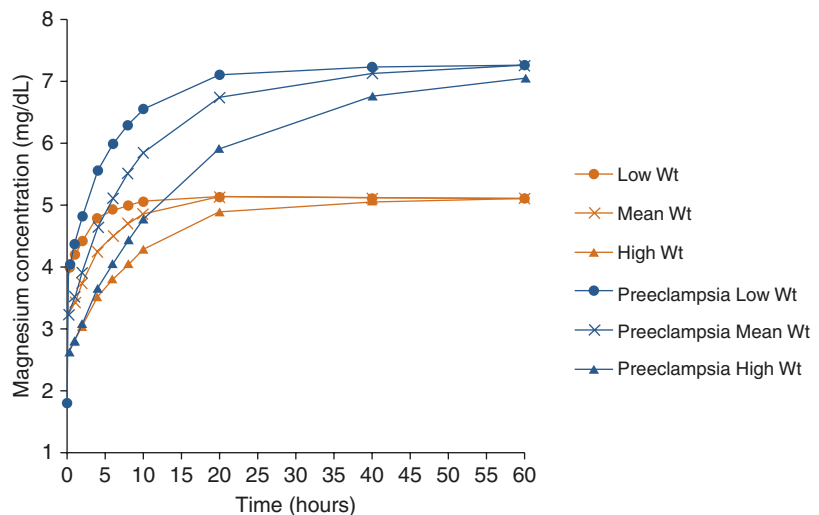
### Renal Colic

Although controversial, magnesium sulfate could have combined beneficial effects in patients with renal colic or renal collecting system rupture [201, 202]:

- tocolysis,
- ureteric muscle relaxation,
- direct pain relief,
- decreased formation and progression of some forms of renal stones.

Ureteric muscle relaxations relieve pain and magnesium sulfate directs pain relief on the molecular level. It is a noncompetitive antagonist of N-methyl-d-aspartate (NMDA) glutamate receptors that participate in pain feeling and persistence. These pain relief effects can result in lesser use of other analgesics. Magnesium is a urinary stone inhibitor because it competes with calcium for oxalate, thus forming a magnesium-

**Fig. 4.11** Magnesium serum concentration after 4 g loading dose of magnesium sulfate, followed by 2 g/h infusion among pregnant women with and without preeclampsia and women of lowest (55 kg), mean (88 kg), and greatest (157 kg) body weights. (Reproduced with permission from [196])



oxalate complex that is more soluble than calcium oxalate [203]. This role could be less important in pregnancy because pregnant women are twice as likely to have calcium phosphate stones than age-matched nonpregnant women and are two to three times more likely to have calcium phosphate stones than oxalate stones [204].

#### 4.6.2.2 Progesterone

##### Adnexal Torsion/Ovariectomy

The tocolysis includes oral or IM progesterone in the first trimester and oral or IV ritodrine in the second and third trimesters [205]. With the ovariectomy during the first trimester, the patient should receive 17 $\alpha$ -hydroxy progesterone caproate 250 mg im. weekly for four weeks as progestogen support for the pregnancy [206] and protection from uterine contractions and PTL. After this period, progesterone is produced by the placenta, and there is no need for its substitution.

There are no data about the specific influence of isolated Fallopian tube torsion on uterine irritability during pregnancy. Therefore, prophylactic tocolysis is unnecessary and should be administered when uterine contractions are present [207].

##### Abdominal Trauma

Instead of magnesium sulfate, slow-released progesterone should also be considered for uterine contractions after abdominal trauma in pregnancy [208].

#### 4.6.2.3 Anti-Inflammatory Agents

##### NSAIDs/Indomethacin

Because bacterially induced PTL is associated with increased prostaglandin production, inhibiting the synthesis of prostaglandins is recommended in cases of (potential) infection-induced PTL. The administration of nonsteroidal anti-inflammatory drugs (NSAIDs) curtails the progression of both term labor and PTL [209, 210]. Currently used NSAIDs, such as indomethacin, block COX-1 and COX-2. Treatment with these

drugs is associated with fetal and maternal side effects that have precluded their use [209, 211]. Prostaglandin synthetase inhibitors were blamed for reversible closure/constriction of ductus arteriosus, with minimal danger when used between 26 and 34 weeks of pregnancy [212, 213]. Although antenatal indomethacin may provide enough time for antenatal steroids to improve fetal maturation, these benefits are associated with periventricular leukomalacia in premature infants [213]. The results also suggest that indomethacin exposure within 72 h before delivery is associated with necrotizing enterocolitis in premature infants. Antenatal indomethacin is not associated with patent ductus arteriosus, respiratory distress syndrome, bronchopulmonary dysplasia, intraventricular hemorrhage, and mortality in premature infants. Also, no teratogenesis [188], altered hematological indices, or transient renal insufficiency [214] were detected.

Observations indicate that COX-2-derived prostaglandins are important for bacterially induced PTL and that COX-2 is a potentially important target for stopping PTL [215]. There are still unresolved issues about the duration and the dosage of selective cyclooxygenase inhibitors on PTL.

One of the drawbacks of prostaglandin synthetase inhibitors is their anti-inflammatory and antipyretic effect, which might mask the clinical presentation of the acute abdomen and give the surgeon a false sense of security. Therefore, it should be used once the diagnosis is established.

##### Experimental Anti-Inflammatory Agents

The following sections consider some promising anti-inflammatory agents potentially used to prevent infection-induced PTL.

##### NF- $\kappa$ B Inhibitors

*N-acetylcysteine* is a nonspecific free radical scavenger and NF- $\kappa$ B inhibitor, but is currently not in clinical use.

*Sulfasalazine*, a salicylate drug that blocks NF- $\kappa$ B activation by directly inhibiting the IKK kinases, is well tolerated and approved in pregnancy, with no discernible increase in the risk of congenital fetal defects and morbidity or mortal-

ity [216]. However, increased levels of chorionic apoptosis have been reported in a human membrane model, suggesting that prolonged treatment may result in eventual membrane degradation and loss of function and structural integrity [30]. Potential use with extrauterine, intraperitoneal (acute abdomen) -induced PTL is its short-course use in addition to antibiotics and infection source control.

#### TLR4 Antagonists

Inhibition using a monoclonal anti-TLR4 antibody was effective in vivo in reducing pro-inflammatory mediator (TNF- $\alpha$ , IL-8, and PGE2) production in amniotic fluid [217] and the incidence of LPS-induced PTL [218]. Alternate TLR4 antagonists include eritoran tetrasodium [219] and TAK-242 [220], neither of which have been examined. TLR4 antagonism is only appropriate in cases of Gram-negative bacteria-induced PTL.

#### Anti TNF- $\alpha$ Antibodies

The complexity of cytokine interactions associated with PTL suggests that targeting individual cytokines may not be the most optimal therapeutic intervention (Fig. 4.11). Interestingly, maternal administration of these agents (infliximab) persists in the neonatal circulation for many weeks after birth [221] and may, therefore, dampen intrauterine and fetal inflammation protecting the fetus from the adverse sequelae of intrauterine infection and inflammation. Also, these agents could be used for treating some of the causes of acute abdomen during pregnancy (Crohn's disease). There is little evidence for congenital abnormalities with anti-TNF- $\alpha$  therapy during pregnancy [222], but high levels in fetal circulation may increase the risk of neonatal infection. These facts should be weighed against the consequences of PTL caused by the acute abdomen.

#### Cytokine Suppressive Anti-Inflammatory Drugs (CSAIDs)

CSAIDs target the NF- $\kappa$ B and p38 MAPK signaling pathways with demonstrated efficacy in animal models [223–225]. These agents can be more effective and selective than NSAIDs in

inhibiting infection-induced PTL. They directly target signaling molecules without interfering with prostanoids' constitutive/homeostatic roles (Fig. 4.12). Depending on the route of administration and placental transfer properties, CSAIDs may potentially block IAI and fetal inflammation, thereby protecting the fetus from the adverse sequelae of exposure to inflammatory mediators.

#### Resveratrol

Resveratrol is a natural polyphenol capable of reducing LPS-induced PTL to 36% (versus 85% without the drug) and stillbirth to 34% (versus 62% without the drug) when administered orally to pregnant mice [227]. The suggested mechanism is the downregulation of the expression of pro-inflammatory mediators such as iNOS and COX-2 in macrophages and suppression of the production of eicosanoids such as prostaglandins. It was not tested on acute abdomen-induced PTL. Trans isoform should be avoided. The reduction in the DNA replication rate is one of the mechanisms by which trans-resveratrol impacts embryoid body development [228].

#### 4.6.2.4 Betamimetics

Betamimetics are not indicated in patients with an acute abdomen. Ritodrine should not be used in a bowel obstruction or toxic megacolon due to its influence on colonic dilation [229, 230].

### 4.6.3 Combination Treatment

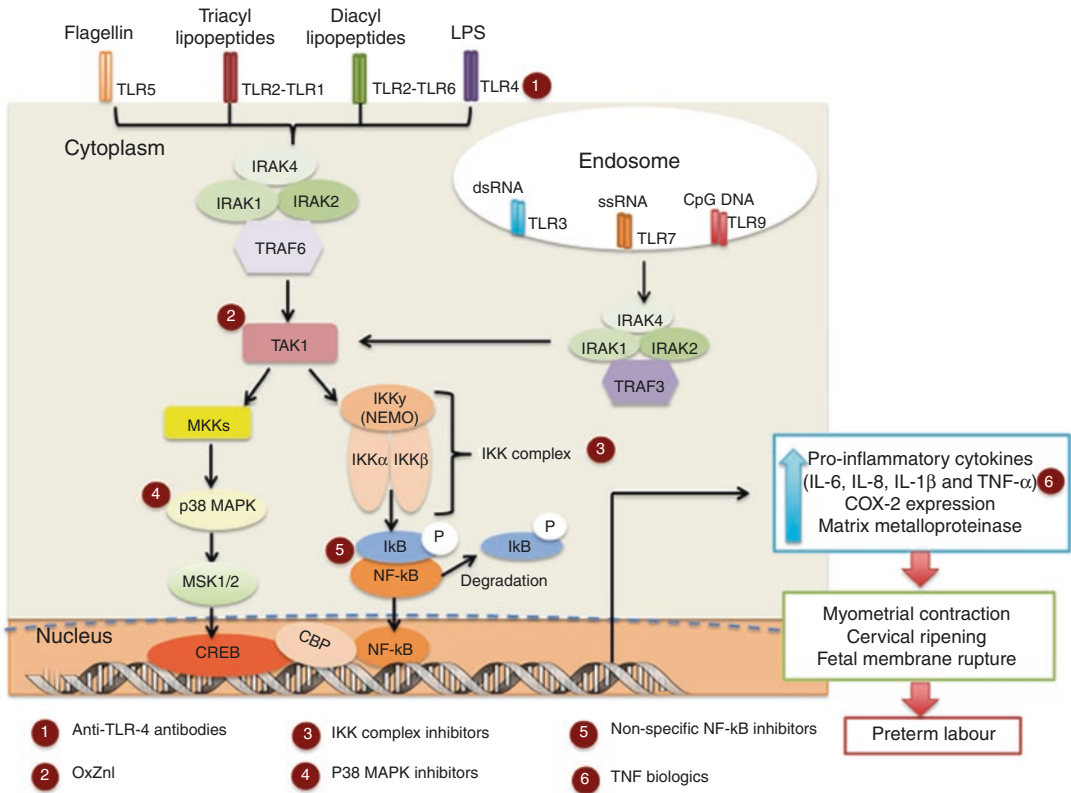
#### 4.6.3.1 Combination Tocolysis

It is unclear whether a combination of tocolytic drugs for PTL is superior to a single-agent tocolysis due to a lack of trials in patients with acute abdomen.

#### 4.6.3.2 Tocolysis and Non-Tocolytic Agents

There is only one study in non-acute abdomen patients. Using rigorous entry criteria, a therapeutic cocktail of interventions, including antibiotics, steroids, and tocolytics, demonstrated neonatal benefit primarily by prolonging gestation [231].





**Fig. 4.12** Infection-induced preterm labor triggered by activation of TLR-mediated NF-κB and p38 MAPK inflammatory signaling cascades. Targets for the selected

anti-inflammatory agents are in red circles. (Reproduced with permission from [226] under the CC BY 4.0)

A single antenatal course consists of  $2 \times 12$  mg betamethasone IM, 24 h apart, or  $4 \times 6$  mg dexamethasone IM every 12 h, after 24 weeks of gestation.

The duration of fetal benefit after a course of glucocorticoids is uncertain. A repeat course might confer a modest additional neonatal benefit, whereas multiple courses can reduce fetal growth [232]. Beneficial effects include a reduced rate of respiratory distress syndrome, intraventricular hemorrhage, neonatal death, necrotizing enterocolitis, patent ductus arteriosus, and bronchopulmonary dysplasia [233].

In patients with acute abdomen, antibiotics are used as indicated for the underlying disease as prevention or treatment.

#### 4.6.4 Placental Abruption Treatment

Immediate CS is indicated with a viable live fetus in traumatic-induced (See Sect. 25.3.6.1) and infection-induced placental abruption.

### 4.7 Prognosis

PTB ranges from 5% of births in European countries to 18% in certain African countries [234]. It is the leading cause of childhood mortality in children under 5 years [235]. All-cause PTB accounts for 75% of perinatal mortality and more than half of long-term morbidity [236]. PTB has an increased risk of cognitive and neurological impairment, such as cerebral palsy and respira-

tory and gastrointestinal complications [4]. There is also an increased risk of chronic diseases in adulthood, such as obesity, diabetes, and hypertension [1]. Interestingly, premature males are at greater risk of mortality and neurological and respiratory morbidity when followed up at 2 years of age [237].

Several critical questions remain unanswered: (1) the identification of a causative infectious agent(s), (2) the role of polymicrobial infection, (3) the critical locus of infection, (4) the burden of infection, and (4) the central immune cells and immune pathways.

Most premature infants exposed to one or more postnatal gram-negative bacteria or coagulase-negative staphylococci, *Staphylococcus aureus*, and group B *streptococcus* are associated with an increased risk of cerebral palsy and adverse neurodevelopmental outcomes at 2 years [238–240]. Fetal bacteremia was found in 33% of fetuses with positive amniotic fluid cultures and 4% of those with negative amniotic fluid cultures in the context of PPROM. Therefore, subclinical fetal infection is far more common than traditionally recognized. Recently, 23% of neonates born between 23 and 32 weeks of gestation had positive umbilical blood cultures for genital mycoplasmas [241].

The fetal mortality rate and the type of fetal morbidity differ between acute and (the type of) chronic maternal abdominal conditions. Acute abdominal conditions mainly result in spontaneous abortion, stillbirth, or PTL, while chronic inflammatory conditions result in congenital anomalies and PTL. Even acute abdominal conditions resemble chronic conditions if treated conservatively, which could result in recurrences with a chronic impact on the fetus.

#### 4.7.1 Fetal Inflammatory Response Syndrome

##### 4.7.1.1 Pathophysiology

Most fetuses exposed to chorioamnionitis develop a systemic inflammatory response known as the fetal inflammatory response syndrome (FIRS) [242, 243]. This is due to the fetus being

in direct contact with the infected amniotic fluid or inflammatory cell transfer from the uteroplacental circulation. FIRS can be clinical or subclinical. *Clinical FIRS* is defined by a fetal plasma IL-6 >11 pg/mL [244], while *subclinical FIRS* is defined histologically by funisitis and fetal vasculitis [243]. Fetuses with elevated plasma IL-6 had a higher rate of severe neonatal morbidity and a shorter cordocentesis-to-delivery interval than those with <11 pg/mL. The disorder can also be diagnosed by measuring CRP in umbilical cord blood. Fetuses with FIRS have more systemic involvement, including hematologic abnormalities (neutrophilia) and a higher median nucleated red blood cell count than those without elevated IL-6. Also, fetal stress is determined by the fetal plasma ratio of cortisol to dehydroepiandrosterone sulfate (DHEAS), congenital fetal dermatitis, fetal cardiac dysfunction, involution of the thymus, and abnormalities of the fetal lung and brain. Among patients with PPROM, elevated fetal plasma IL-6 is associated with the impending onset of PTL, regardless of the inflammatory state of the amniotic fluid. This suggests that the human fetus plays a role in initiating the onset of labor.

However, maternal-fetal cooperation must occur for parturition to be completed. Fetal inflammation has been linked to the onset of labor associated with ascending intrauterine infection. However, systemic fetal inflammation may occur in the absence of labor if the inflammatory process does not involve the chorioamniotic membranes and decidua. Such instances may take place in the context of hematogenous viral infections or other disease processes (e.g., rhesus alloimmunization).

Affected fetuses have evidence of multiorgan involvement with a higher rate of severe neonatal morbidity after adjustment for gestational age, and PPROM results in a shorter cordocentesis-to-delivery interval. Neutrophilia is present in two-thirds of fetuses with FIRS, whereas neutropenia in 7%. FIRS is associated with BPD. The fetus can inhale amniotic fluid and its contents which can reach the distal parts of the airways and the alveoli. FIRS is found in 76% of infants with atypical chronic lung disease, defined as chronic

lung disease without respiratory distress syndrome. Bacterial products and cytokines may contribute to myocardial depression. Fetuses that cannot modify their cardiac compliance or maintain ventricular cardiac output may suffer inadequate brain perfusion, predisposing them to hypotension and brain ischemia in utero. This can result in periventricular leukomalacia and brain injury.

#### 4.7.1.2 Prevention and Treatment

Treating maternal bacterial infection eliminates potentially inoculated bacteria in the fetus or amniotic fluid. There is no effective treatment to prevent infection/inflammation-related fetal brain injury. Prophylactic antibiotics given to mothers at risk of PTL who have ruptured membranes are still associated with an increased risk of fetal death and disability [245]. Killing bacteria will release even more inflammatory bacterial fragments and, in addition to hypoxia and hyperthermia, could result in brain injury despite prophylactic antibiotics.

Inhibitors of the IL-1RI decrease proinflammatory cytokine IL-1 $\beta$  production, curbing the inflammatory process. The commercially available drug anakinra (Kineret) competitively blocks the receptor and inhibits all its intracellular pathways [246]. It protects the fetal brain from inflammatory damage [247].

### 4.7.2 Fetal Mortality

#### 4.7.2.1 Fetal Infection

In 1912, it was observed that the infection might extend to the uterus from the Fallopian tubes, the broad ligaments, and then from the uterine wall to the placenta [248]. With diffuse peritonitis, transplacental bacterial diffusion could result in intrauterine fetal death [249]. Fetal microbial invasion results in FIRS that can progress toward multiple organ dysfunction, septic shock, and death without timely delivery. Due to the small number of patients, it is difficult to compare the influence of therapeutic delay, the type of microorganism involved, and the proven route of infection. It is questionable whether acute

chorioamnionitis has enough time to develop in the acute abdomen. Also, cases of subclinical chorioamnionitis are missed resulting in an underestimation of this condition.

The risk of fetal death from maternal pyrexia, distinct from infection, may have been overstated [250]. Some drugs for treating severe infections may be teratogenic, thus compounding the effect of pyrexia. For effects of maternal pyrexia on fetal and neonatal development, see Sect. 4.7.3.

#### 4.7.2.2 Fetal Trauma

See Chap. 5.

#### 4.7.2.3 Placental Abruption

For fetal outcome from traumatic placental abruption, see Sect. 25.3.6.1. Neonates of the placental abruption with histologic chorioamnionitis group had increased neonatal adverse outcomes than the group with placental abruption from chronic vascular insufficiency on the maternal-fetal interface [251]. No comparisons of placental abruptions exist between specific intra-abdominal infections or maternal abdominal trauma. Placental abruption rate from specific acute abdominal causes is described in the chapters dealing with these conditions.

### 4.7.3 Fetal Morbidity

The type of fetal morbidity partly depends on the cause of the maternal acute abdomen. There are three distinctive etiologic groups: (1) IAI, (2) bleeding, and (3) direct or indirect fetal trauma. Also, the presence of these etiologic groups makes both maternal and fetal prognoses worse. Fetal injuries common for all etiologic groups are described. For specific fetal traumatic injuries, see Chap. 5.

#### 4.7.3.1 Brain Injury

Perinatal brain injuries, particularly cerebral palsy, periventricular leukomalacia, and intraventricular hemorrhage, are linked to intrauterine inflammation [252–254]. Exposure to histological chorioamnionitis combined with impaired placental perfusion increases the risk of poor

neurological and neurocognitive outcomes at 2 years [255] and 8 years [256] of corrected age in children born very preterm. Histological chorioamnionitis is also associated with increased speech delay and hearing loss at 18 months of corrected age in infants born very preterm [257]. Furthermore, histological chorioamnionitis caused by bacterial and viral infection has increased the risk of autism and schizophrenia [258]. Schizophrenia may result from post-acute latent inflammation, whereas autism may be due to persistent inflammation [258].

Several potential mechanisms could connect chorioamnionitis and adverse neurological outcomes. Intrauterine inflammation is linked with diffuse white matter injury in the brain of preterm neonates due to TNF- $\alpha$  signaling and has been described as toxic to developing oligodendrocytes [124, 259, 260]. Chorioamnionitis has been associated with impaired fetal and newborn cardiac function [261, 262], which may compromise brain blood flow due to lower blood pressure [261, 263, 264]. This results in altered cerebral oxygen delivery. Impaired cerebral autoregulation is considered one of the main contributors to brain injury in preterm neonates [253, 265]. Impaired cerebral autoregulation may be more prevalent in neonates born after exposure to intrauterine inflammation [264, 265]. Data from animal experiments are consistent with human studies in showing the effects of intrauterine inflammation (with various routes of microbe inoculation) on the developing brain in the form of (1) karyorrhexis (nuclear fragmentation) of glial cells and reduced density and disorganization of white matter [266], (2) astrocytosis and a reduction in oligodendrocyte number in subcortical white matter [267], (3) diffuse damage and focal periventricular leukomalacia [268], and (4) decrease in myelination, potentially due to reduced numbers or function of oligodendrocytes [269]. Currently, it is unknown whether the: (a) location of the primary infective focus, (b) the route of infection dissemination, or (c) duration and severity of infection have different central nervous system (and other organs) consequences.

Women who experience abdominal trauma have an increased incidence of birth defects,

mostly damage/defects of the central nervous system, especially hydrocephaly [270, 271]. In 2 out of 7 blunt abdominal traumas, movement disorders and cerebral palsy were detected [270, 272].

### Cerebral Palsy

Although previously described, in 1861, William John Little (Fig. 4.13), an orthopedic, described the association of prematurity with cerebral palsy and the development of spastic diplegia. He hypothesized that, even without apparent external trauma, an inadequate supply of “oxygen and materials for nutrition” from the placenta to the fetus or an “insufficient removal of carbon and other residues” from the fetus through the placenta could lead to brain injury [273]. One-third of all neonates who later have signs of cerebral palsy weigh less than 2500 g. Newborns with birth weights less than 1500 g have a rate of cerebral palsy 25–31 times higher than those with normal birth weights. The most common form of cerebral palsy affecting preterm babies is spastic diplegia. In turn, preterm babies who develop spastic diplegia have a high rate of periventricular leukomalacia.

### Infection/Inflammation

In 1955, Eastman and Deleon observed that intrapartum maternal fever was associated with a sev-



**Fig. 4.13** William John Little ((1810–1894), an orthopedic surgeon, lectured at the *Obstetric Society of London* and accentuated the association of prematurity with cerebral palsy in *Lancet* in 1861. (Reproduced with permission from [280])

enfold increase in the risk of cerebral palsy [274]. The prolonged temperature rise increases the metabolic rate and the oxygen requirements of the fast-developing tissues. When the demand outstrips the supply, placental efficiency diminishes. Also, fast-growing tissues are especially susceptible to noxious stimuli [275]. For each degree of body temperature over 37 °C, the oxygen required for tissue metabolism, including the brain, rises by 7%. Therefore, an intrapartum infection is a cause of cerebral palsy through the effects of bacterial toxins and the mechanism of hypoxia/anoxia. In 1977, chorioamnionitis increased the risk of cerebral palsy among low-birth weight infants from 12/1000 to 39/1000 live births [276].

### Trauma

William Osler, who coined the term cerebral palsy, favored the hypothesis that trauma leading to meningeal hemorrhage and brain and spinal cord compression was a major cause of cerebral palsy [273]. The risk of cerebral palsy after MVA is 1.8/1000 [277]. MVAs during pregnancy may be associated with an increased risk of cerebral palsy in neonates with PTB [277]. Possible mechanisms for the association between pregnancy trauma and cerebral palsy include reduced placental blood flow, placental embolization, and placental abruption. Kleihauer-Betke testing at the time of trauma and histological examination of the placenta at the delivery might clarify the role of placental separation [278]. The correlation between the type of cerebral palsy and maternal trauma during pregnancy is not clarified, but the spastic form is predominant in term infants [279]. In term babies, the type of MRI abnormality corresponds with the timing of the antenatal injury: trauma at 20 weeks results in extensive cortical dysplasia; trauma between 24 and 30 weeks results in periventricular white matter abnormality; trauma after 30 weeks results in cystic encephalomalacia [279].

### Epilepsy

Epilepsy is childhood's most common severe neurologic disorder [281–283]. Before the age of 15, 1–1.7% of all children will have at least one unprovoked seizure, and up to 0.8% will have

repeated seizures [282]. The incidence of childhood epilepsy is highest in the first year of life—150/100,000 person-years, falling to 50/100,000 person-years after the age of 9 [282].

Generalized epilepsies can often be traced to infection [282]. In particular, insults acting during the prenatal and to single-gene mutations or chromosomal abnormalities, while partial epilepsies are frequently triggered by external insults to the central nervous system, including brain injury and central nervous system neonatal period, are thought to contribute to some types of epilepsies [281, 282, 284]. A seasonal pattern, i.e., an excess of births during winter months among children who develop epilepsy [285, 286], suggested prenatal exposure to maternal infection may be a risk factor. Any maternal infection during pregnancy (method of measurement unspecified) was associated with a 1.0- to 1.6-fold increase in the risk of childhood epilepsy [284]. Maternal self-reported history of cystitis, pyelonephritis, vaginal yeast infection, or symptoms of infection (diarrhea, coughs) during pregnancy was associated with a 1.2- to 2.6-fold increased risk of epilepsy among offspring [287]. Risk varied by type of infection and was the highest for a self-reported vaginal yeast infection (2.6-fold) and pyelonephritis (2.3-fold) [287]. Therefore, a 40% increased risk of epilepsy is associated with prenatal exposure to maternal systemic infection [288]. The infection could be caused by its antecedents, consequences, or antibiotic treatment. However, the similar magnitude of increased risk observed for different types of antibiotics argues against the role of specific types of infections or specific therapies. Various maternal infections, measured by self-report collected twice during pregnancy and 6 months after delivery, were associated with epilepsy in offspring [287].

Children with prenatal exposure to more than two maternal fever episodes, maternal fever with urinary symptoms, or maternal fever of 39 °C have an increased risk of epilepsy—suggesting that the underlying causes of fever rather than elevated temperature, such as sauna use, play a role [289]. Inflammation may be involved in linking fever and epilepsy [290]. Inflammatory reactions in the brain can enhance neuronal



excitability [291], and anti-inflammatory treatments reduce seizures in experimental models.

Cytokines are key players in the modulation of neuronal excitability, leukocyte recruitment, and inflammatory central nervous system infections [290], yet their role in the pathogenesis of epilepsy is unclear. In response to infection during pregnancy, maternal cytokine production may induce fetal neurological injury [292]. A nearly threefold increased risk for epilepsy among children born to mothers with epilepsy suggests that infants genetically predisposed to epilepsy may be more susceptible to inflammatory reactions [288].

Premature births result in 75% of neonatal deaths and most neonatal intensive care unit admissions [293]. A substantial effect of premature birth on long-term physical and mental health is observed [294]. Babies born at <28 weeks gestational age spend 85 times longer in the hospital than babies born at term [295]. Even among babies born after 32 weeks, educational and behavioral problems can occur in 33% at 7 years of age [296], with 25% born between 32 and 35 weeks of gestational age requiring nonteaching assistants at school [297].

#### 4.7.3.2 Lung Injury

IAI is also associated with lung injury. Elevated levels of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, and IL-8 in the amniotic fluid have been found in women who had babies with bronchopulmonary dysplasia (BPD), a chronic lung disease affecting infants. There are no data about fetal lung injury associated with acute extrauterine IAI.

#### 4.7.3.3 Low Gestational Weight and Birth Defects

Low birthweight is associated with poor outcomes in cognitive function, academic achievement, behavior, and social adaptation [298, 299]. Low birthweight is also associated with an increased risk of cardiovascular and chronic diseases [300].

#### Domestic Violence

Minor trauma during pregnancy may lead to the subclinical chronic placental disruption that per-

sists during pregnancy, which may cause an increase in the risk for induced abortion, acute placental abruption, PTL, PPRM, and placental insufficiency that restricts fetal growth and lower Apgar score [301].

1/3 of the studies reported a positive association between intimate partner violence and low birth weight or PTB [302–304]. Rates of low birth weight among battered women were 1.5–2.5 times higher [302–304] than those among nonbattered women, and rates of PTB were 2.5–4 times higher [302–304]. Others lacked sufficient power to address most pregnancy outcomes [305, 306]. Many studies have reported increased rates of low birth weight, reduction in mean birth weight, or PTL in bivariate analyses. However, the associations became nonsignificant when adjusted for tobacco use and other substances [307, 308].

Stratification by intention suggests three associations - longitudinal limb deficiency, gastroschisis, and hypoplastic left heart syndrome—possibly driven by intentionally inflicted injuries [309]. The majority of intentional injuries result from intimate partner abuse, and these types of injuries could be more stressful for the mother [310].

#### Motor Vehicle Accidents

The estimation is that 9% of survivors of serious crashes develop significant post-traumatic stress symptoms and that many other survivors have post-traumatic stress disorder-like reactions [311]. Associations have been observed between maternal stress during pregnancy, especially during the periconceptional period and conotruncal heart defects, interrupted aortic arch type B, atrioventricular septal defect, pulmonary atresia, tricuspid atresia, hypoplastic left heart syndrome, anorectal atresia/stenosis, longitudinal limb deficiency, gastroschisis, neural tube defects [312, 313], and orofacial clefts [312, 313]. One should be cautious with conclusions because there is a higher prevalence of alcohol and cigarette use during pregnancy among women who reported an intentional injury [310]. Alcohol and cigarette use during pregnancy is associated with an increased risk of birth defects [314, 315].

One thread suggests that stress, either very early in pregnancy or in the 24–28th weeks of pregnancy, leads to a twofold increase in the risk of autism [316]. Since autism is usually not apparent until 1–3 years of age, it may be difficult to trace back to the primary events.

#### 4.7.4 Maternal Outcome

In the late nineteenth century, maternal and fetal mortality from maternal diffuse peritonitis was 100% [130, 317].

##### 4.7.4.1 Placental Abruption

Maternal mortality associated with all-cause placental abruption decreased from 8% in 1919 to <1% in 1995 [318]. After placental abruption with a survived newborn, 59% of women had a subsequent delivery, compared with 71% of those without abruption. After the perinatal loss, the corresponding rates were 83 and 85% [319]. This may reflect maternal anxiety and distress from further pregnancies caused by prior placental abruption. For trauma-induced placental abruption outcomes, see Sect. 25.3.7.2.

##### 4.7.4.2 Intrauterine Fetal Death

The issue with intrauterine fetal death is whether to deliver on an emergent basis by CS or wait for spontaneous delivery. The argument for late spontaneous delivery is avoiding CS with all its potential complications without benefit for the dead fetus. On the contrary, intrauterine retention of a dead fetus for >5 weeks may result in potentially hazardous hypofibrinogenemia in 25% of patients. Prolonged retention is unusual since spontaneous delivery occurs within 3 weeks of fetal death in >90% of patients [320]. If hypofibrinogenemia develops, the onset is gradual. At least before the delivery, it may be asymptomatic or show clinical evidence of abnormal hemostasis, such as gingival bleeding or extensive ecchymoses. If hypofibrinogenemia develops, it persists until the uterus is emptied. Fibrinogen administration has a transient effect and can result in hepatitis.

There is no indication for emergent delivery before 3 weeks after fetal death, but not longer than 5 weeks [320] if there are no maternal indications for emergent delivery.

##### 4.7.4.3 Intra-abdominal Infection

A CS due to IAI exposes the uterine wound to infection. This can result in endometritis, increasing the risk of opening the hysterorrhaphy [321]. Moreover, such uterine scars transform subsequent pregnancies into high-risk pregnancies for uterine rupture.

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## Abstract

The fetus can sustain mechanical trauma during pregnancy or difficult delivery. Approximately 2% of all live births in the USA were exposed to intrauterine trauma from motor vehicle accidents. Blunt fetal trauma during pregnancy can result in (1) fetal/neonatal death, (2) direct fetal injury, and (3) deceleration injury. It can be detected during maternal imaging diagnostics, CTG monitoring, or delivery. It can also be the result of childbirth trauma. It is imperative to detect intrauterine trauma because, in many cases, it indicates Cesarean delivery to minimize additional trauma during difficult or prolonged vaginal delivery. The fetal outcome depends on the underlying fetal, amniotic, and uterine injuries. Penetrating fetal trauma accounts for 10% of all fetal trauma. With penetrating trauma, primarily stab injuries in the second half of pregnancy, maternal injuries are minimal due to the protective role of the pregnant uterus. Consequently, fetal penetrating trauma is common. With stabbing fetal trauma, mortality is minimal, with the potential for various degrees of impairment. On the contrary, gunshot trauma has high fetal mortality from direct fetal trauma or indirectly from severe maternal bleeding.

## 5.1 Fetal Physiology

During the first week, the conceptus has not yet been implanted in the uterus, making it relatively resistant to injury. Soon after, the embryo attaches to the uterus via the anchoring villi. The placenta is not as elastic as the myometrium, potentially leading to shear stresses and disruption of the villi with force applied to the uterus. The fetus's well-being depends on the adequacy of the maternal blood flow to the placenta, mainly derived from the uterine arteries. The uterine vascular bed is a low resistance system, not capable of further dilation and devoid of autoregulation. Therefore, placental blood flow varies directly with the net perfusion pressure (uterine artery pressure-uterine venous pressure) across the intervillous space and inversely with uterine vascular resistance. In normal pregnancy, the fetus has a considerable functional reserve to withstand uterine blood flow or oxygenation changes. In sheep, fetal oxygen consumption does not decrease until oxygen delivery is reduced by 50% [1]. Later in pregnancy, vital fetal organs such as the brain and myocardium are further protected by the "diving reflex," which allows redistribution of fetal cardiac output during maternal hypoxemia or compromised uterine perfusion. The fetus's response to these insults is limited and seems to vary with gestational age. Decreased placental blood flow quickly leads to fetal distress.

The feto-placental circulation contains around 110 mL/kg of blood [2]; at 30 weeks gestation, about 55 mL/kg is in the fetus, rising to 90 mL/kg at term. Therefore, premature infants have a lower blood volume, and the consequences of bleeding present earlier. Maternal exposure to fetal blood cells during gestation (feto-maternal hemorrhage—FMH) is common, occurring in 95% of pregnancies. However, the exposure volume is small, with <2 mL in 98% of exposures [3]. In rare cases, in 0.3% of pregnancies, fetal hemorrhage ( $\geq 30$  mL) occurs, and 1:2,800 pregnancies are complicated by a massive fetal blood loss ( $\geq 150$  mL), causing fetal hemodynamic instability [3, 4].

## 5.2 Blunt Fetal Trauma

### 5.2.1 Incidence

Approximately 2% of all live births in the USA, or 79,000 children (26/1,000 person-years), were exposed in utero to police-reported motor vehicle accidents (MVA) [5]. A significant increase in exposure may have resulted in a poorly documented trauma-induced epidemic of fetal loss, fetal injury, and adverse reproductive outcomes. There is indirect corroborating evidence from national vital statistics data of similar increases in neonatal deaths due to maternal trauma during this period [6], without the possibility of confirmation because of documentation problems. The NHTSA reports that only about 23,188 infants are reported with MVA yearly (6/1,000 person-years) [5]. Given the potential number of exposed fetuses, longitudinal research on nonfatal fetal outcomes is needed. Fetal trauma exposure has received very little attention among reproductive and environmental scientists and funding agencies. This is mainly due to (1) major deficiencies in the way fetal trauma-related deaths are coded in vital statistics, (2) the lack or poor quality of pregnancy status variables and follow-up in most injury surveillance systems, (3) unfamiliarity by many reproductive health researchers with injury science and the enormous societal burden of injury, and (4) the difficulty of attributing adverse

birth outcomes and developmental problems many months or years after the trauma. However, the recent convergence of several research lines suggests why this problem should receive urgent attention.

Skull fractures with intracranial hemorrhage appear to be the most common fetal injuries from blunt trauma [7]. Traumatic subdural hematomas (SDH) start from 24 weeks of gestation and are the most common intracranial type of bleeding [8].

### 5.2.2 Pathophysiology

The fetus can sustain mechanical trauma during pregnancy or difficult delivery. There are both maternal and fetal adaptations for exceptional protection during pregnancy. *Fetal adaptation* includes a fast-growing organism with (1) maximal potency of all-tissue regeneration and (2) low bone mineralization rate minimizing both birth and external bone trauma. *Maternal adaptation* includes anatomical and physiological changes in pregnancy that contribute to additional external fetal protection (see Sect. 25.1.3.1).

According to the mechanism and the severity, blunt fetal trauma during pregnancy can result in (1) fetal/neonatal death, (2) direct fetal injury, and (3) deceleration injury. Fetal or early neonatal death results from (1) violent trauma with fetal injuries resulting in fetal death or (2) injury to the feto-maternal unit indirectly causing fetal death. These feto-maternal unit injuries most commonly include placental abruption (see Sect. 25.3.6.1), preterm labor (see Sect. 4.3.3), or traumatic uterine rupture (see Sect. 10.2).

Intrauterine fractures should not automatically be attributed to maternal blunt abdominal trauma. Several etiologic groups [9] can cause intrauterine fractures (Table 5.1). Fetal conditions prone to intrauterine fractures could result in fetal fractures with minimal or even without maternal trauma. Some idiopathic causes result from domestic violence or unawareness of minor trauma.



### 5.2.2.1 Direct Fetal Injury

Direct fetal injuries and fractures complicate <1% of severe maternal blunt abdominal trauma, most commonly during late pregnancy. Most intrauterine fractures occur in the third trimester when the fetal skeleton has reached a substantial size, and the bones have mineralized [13, 14]. The susceptibility of individual fetal bones to intrauterine fracture is generally related directly to the mechanism of injury. Direct fetal injury is relatively infrequent in the absence of uterine injury [15].

Cranial injuries, including subgaleal hematoma (Fig. 5.1), are the most frequent direct fetal

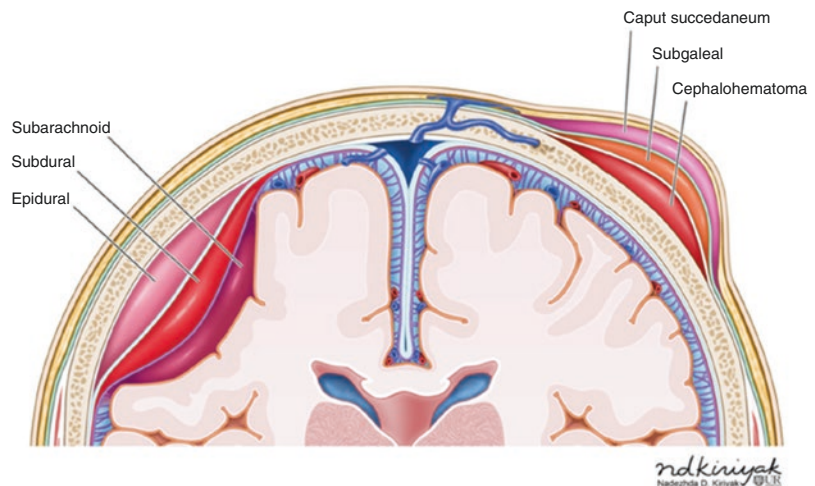
injury after maternal blunt abdominal trauma. In early pregnancy, the uterus is protected by the bony pelvis and the amniotic fluid, which act as a hydraulic shock absorber, decreasing the force of the blow by transmitting it equally in all directions. Later in pregnancy, the fetal head is fixed in the pelvis, and the buffering effect of the amniotic fluid is decreased, making the head prone to injury. Depressed skull fractures occur due to the contact of the skull against the promontory of the sacrum [10] or anterior pelvic ring. Most intrauterine skull fractures are related to a severe maternal injury involving pelvic fractures [16], although not always [17, 18]. Fetal skull fractures should be considered an index injury for severe maternal trauma. Vice versa, multiple pelvic fractures in pregnant women require a thorough sonographic (US) and radiographic examination of the uterus and fetus.

Brain injury can result from direct and indirect (deceleration) injuries in later pregnancy. Fetal brain and skull injuries may be more common in fetal head engagement during maternal pelvic fractures [20, 21]. In these direct injuries, either the maternal abdominal wall is struck by a blunt instrument, or the maternal abdomen strikes the car's dashboard, steering wheel, or another area. Such injuries may be missed at the time of the accident, and the pregnancy may continue to term in the absence of concomitant placental or uterine injuries. Both brain (vessel) and skull injuries could be isolated or associated. When

**Table 5.1** Causes of intrauterine fetal fractures [9–12]

|                                             |
|---------------------------------------------|
| Maternal abdominal trauma                   |
| Fetal skeletal dysplasias                   |
| Osteogenesis imperfecta                     |
| Osteopetrosis                               |
| Ehlers-Danlos syndrome                      |
| Maternal metabolic/biochemical disturbances |
| Vitamin D deficiency                        |
| Malabsorption                               |
| Osteomalacia                                |
| Hyper-/hypoparathyroidism                   |
| Steroids?                                   |
| Fetal vascular injury                       |
| Compression                                 |
| Thromboembolism                             |
| Idiopathic                                  |
| Combination                                 |

**Fig. 5.1** Hemorrhage by location within the different layers of the meninges (*left*) and scalp (*right*). (Reproduced with permission from [19] under the CC BY 4.0)





comparing epidural and SDH, almost all were SDH [8]. The distribution of blunt maternal trauma mechanisms causing fetal SDH is MVA in 69%, domestic violence in 23%, and the remaining were undefined [8]. Due to a small number of patients, it is difficult to conclude the influence of seat belts and airbags deployed on fetal SDH. Hemosiderin deposition in brain hemorrhage should be evaluated because its presence confirms an old (chronic) bleeding. It is present for some time before intrauterine death. MacDonald et al. in 1977, first described this phenomenon [22].

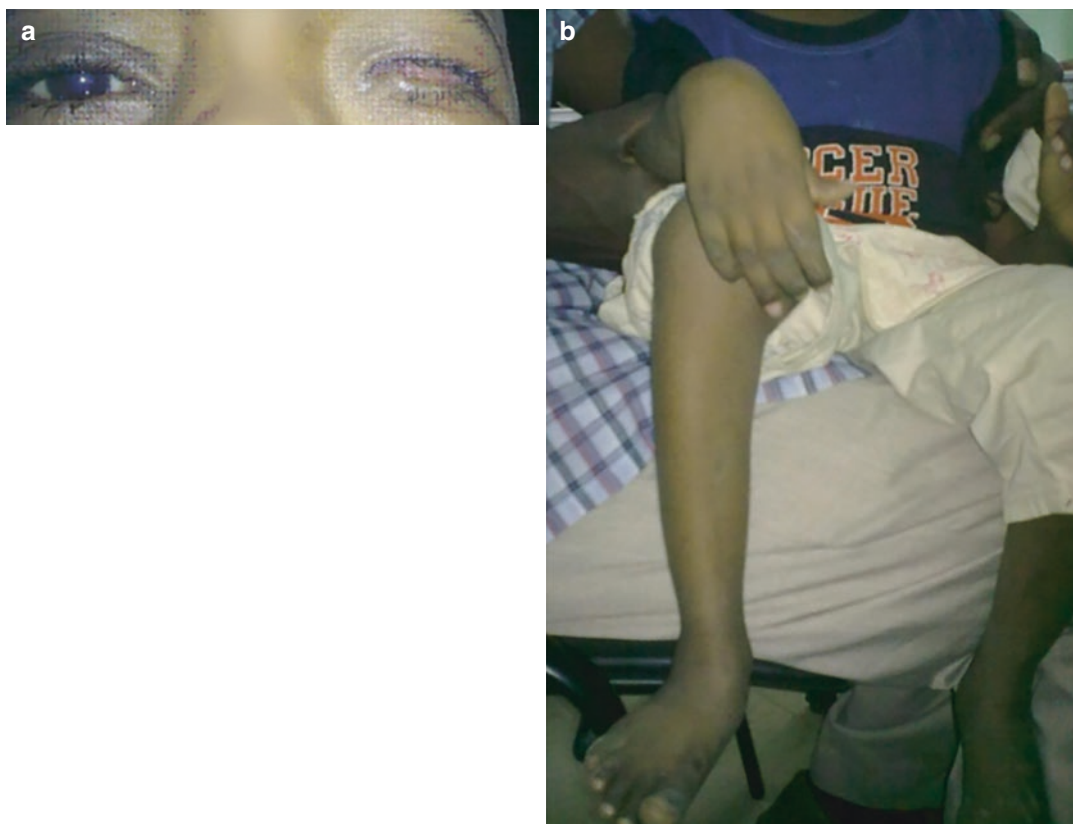
Isolated fractures of the mandible, the clavicle, the vertebrae, and long bones have been reported [23].

Severe extraskeletal fetal injuries are extremely rare but can result in significant child

disabilities. Such injuries include traumatic loss of an eye (Fig. 5.2a) or neurologic impairment, causing less functional extremities or even palsy (Fig. 5.2b).

Traumatic maternal uterine rupture is commonly associated with a direct fetal injury. During pregnancy, uterine blood flow increases tenfold—from the nongravid rate of 60 cm<sup>3</sup>/min to 600 cm<sup>3</sup>/min at term [13]. Acute maternal blood loss is partly compensated by increased uterine vascular resistance and decreased blood flow [25]. Therefore, the hemodynamic stability of the mother is maintained at the expense of uterine blood flow, putting the fetus at risk [15, 26].

Neonatal long bone fractures at birth occur after difficult deliveries (especially femur fractures with breech presentation), mainly during Cesarean section (CS) [27]. Forced obstetric



**Fig. 5.2** At 36th-week gestation, the mother hit herself with the woody part of an axe nonintentionally, resulting in (4-years-old child) (a) neonatal eye damage and (b)

right-sided hemiplegic spastic cerebral palsy and epilepsy. (Reproduced with permission from [24] under the CC BY 2.0)

maneuvers during CS, such as excessive stretching of the legs and bending the femurs during the delivery of the head, may result in fractures. Also, CS breech delivery of the large fetus and the fetus of gestational diabetic mothers necessitate more twisting and pulling, resulting in fractures. In these cases, lower segment transverse uterotomy could be insufficient, and a small vertical incision is needed. Additional vertical incision enables less force for the delivery, especially the fetal head [28].

Spontaneous femur fractures are exceedingly rare and should be included in the differential diagnosis. All spontaneous femur fractures include the mid femur, usually in males in the second half of pregnancy, and on the right side. Low estradiol levels might lead to a corresponding weakness in the male fetal femur. Another mechanism could result from differences in growth, as the femoral shaft develops faster than both ends, making this site more fragile. Also, the fracture site might be related to the intrauterine position of the femur as the right femur always lays over the left femur, which could result in a lever/fulcrum effect [29].

#### 5.2.2.2 Indirect Fetal Injury

In the absence of visible external trauma, indirect injury of the fetal viscera represents deceleration, blast injury, or ischemic, mostly brain injury.

*Deceleration injury* can occur in any fetal part or organ, including an unengaged fetal head [13, 14], spleen [30], liver, kidney, and adrenal gland, causing contusions and hemorrhage [31]. The injury is primarily the result of rapid compression and the impact of the organs during deceleration. It is debatable whether it results from a countercoup effect within their attachments or secondary to a shearing force within the organs [32]. Intrauterine SDH is the result of shearing or acceleration/deceleration forces because of the following features [33, 34]: (1) the head is large and neck muscles weak; this allows more rotational movement with angular acceleration, (2) the subarachnoid space is larger, allowing the brain to move within the skull easily, and (3) the fetal brain has a higher water content that increases its mass and allows it to develop more

momentum when acceleration is applied [33, 34]. These unique conditions could make the fetus more susceptible to SDH even without apparent trauma. The breech presentation places the fetus at higher risk of this type of injury even without skull fractures. It is possible that with a cephalic presentation, the fetal head may be better protected and less mobile within the bony pelvis and, therefore, less susceptible to acceleration/deceleration [35].

*Blast injury* is associated with trauma to the fetal thorax and abdomen. The suggested mechanism of injury is similar to an underwater blast injury, with the shock waves transmitted through the amniotic fluid exerting their effects on the fetus [36].

*A hypoxic insult causes ischemic brain injury* to the developing fetal brain at the time of the traumatic event, either from (1) maternal hypotension, (2) placental embolus [37], or (3) maternal stress. Maternal stress causes catecholamine discharge leading to uterine artery spasms and decreased fetal blood flow [38]. This potential mechanism for ischemic damage after an MVA can occur even without maternal injury [39]. The brain is the most susceptible even to short ischemic periods, which is the reason for more frequent ischemic damage compared to other organs.

#### 5.2.2.3 Childbirth Trauma

Birth trauma, either during vaginal breech delivery [40] or CS (especially with breech presentation) and maneuvers such as external cephalic version [41], can result in fetal injury. Long bone fractures are documented in 0.02% and fetal injury in 1.1% of CS [42]. The highest risk of fetal injury is during CS performed after an unsuccessful trial of vaginal delivery [40] and breech delivery of high birth weight fetuses [43]. Ancient Egypt text does not describe traumatic fetal injury except childbirth trauma [44].

### 5.2.3 Clinical Presentation

#### 5.2.3.1 Intrauterine Trauma

An intrauterine fetal examination is challenging. Pathological findings during maternal abdominal

examination raise the possibility of fetal injury. These include abdominal wall bruises, seat belt signs, deformed uterus, and palpable fetal parts outside the uterus. The maternal seat belt sign strongly predicts severe fetal injury and correlates with fetal transection [45, 46].

Cardiotocography confirms fetal distress as an indirect sign of severe fetal injury.

### 5.2.3.2 Birth Trauma

In newborns with maternal abdominal trauma during pregnancy, careful maternal history and newborn examination are essential. Signs of femur fracture in a newborn are soft tissue swelling, knee stiffness, focal tenderness, and irritability. Signs often appear on the second or third day of life [28]. Limb-sparing is the consequence of extremity fracture or neurological impairment. Extremity deviations or angulations result from birth trauma or a recent intrauterine fracture. A palpable lump on the bone surface is probably due to callus formation.

The absence of external trauma on the newborn does not exclude intracranial or truncal injuries. Even when placental abruption is confirmed with fetal distress, the postdelivery newborn examination is mandatory to exclude potential life-threatening injuries [47].

Maternal plain abdominal X-ray is eventually a babygram that leads to accurate prenatal diagnosis [50], although specific plain X-rays for identifying fetal skeletal pathology exist [51]. A fetal X-ray helps evaluate the axial skeleton, which may be difficult to assess with US. However, unpredictable fetal positioning or maternal-fetal skeletal overlapping lowers the diagnostic accuracy of either of these modalities. If the intrauterine fracture is confirmed by imaging modality, a postnatal X-ray is mandatory to define a need to correct the fracture and follow-up.

Screening 2D US has a sensitivity of 60% [52, 53], while 3D US has a sensitivity of 80% for all skeletal changes [54, 55]. 3D US has an absolute advantage in diagnosing the morphology of the spine and pelvis. Obstetric US enables intrauterine visualization of fetal SDH before the onset of delivery, spontaneously, or after trauma.

A fetal intracranial bleeding/hematoma is not always evident on the initial US, especially early after the traumatic event. Therefore, repeated US several days after trauma (Fig. 5.3) could be diagnostic, especially if there is a transient loss of fetal heart rate variability [48, 49]. The same principle applies in the early puerperium [56].

## 5.2.4 Diagnosis

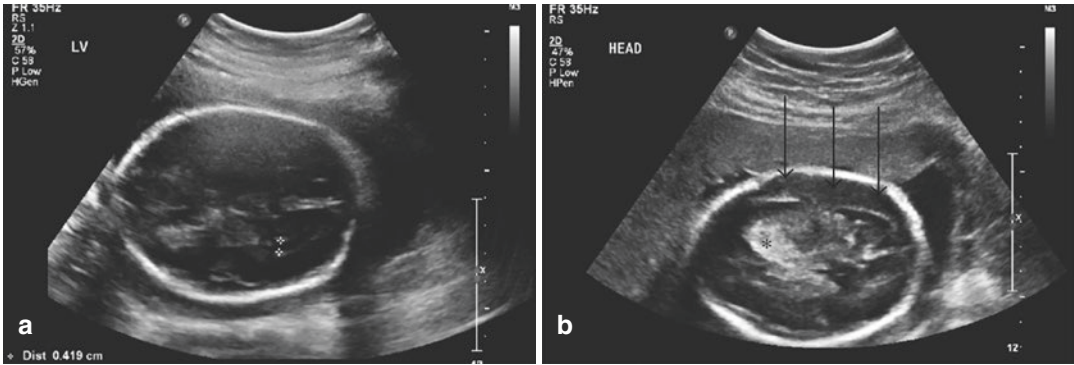
Diagnosis can be made in utero with the continuation of pregnancy without fetal distress (see Sect. 25.3.8.4 for fetal monitoring) or after delivery.

### 5.2.4.1 Intrauterine Diagnosis

If maternal trauma is minor without the indication for imaging diagnostics, abnormal CTG patterns can be the first sign of fetal trauma. Fetal heart rate abnormalities have been associated with fetal intracranial hemorrhage, including decreased fetal heart rate variability and a sinusoidal pattern [48, 49].

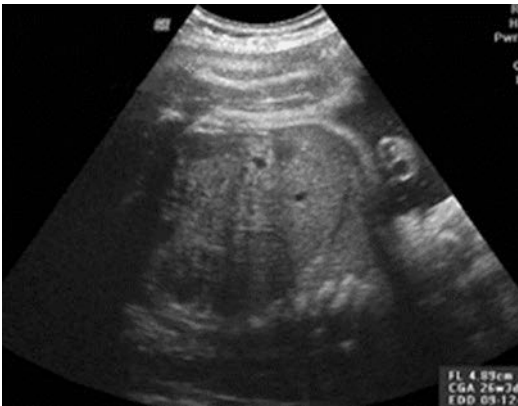
Most abruptions occur within 2–6 h after injury, and almost all within the first 24 h post-injury [57]; therefore, repeated US after several days can also exclude abruption as a cause. With fetal distress, US can rule out other causes of fetal distress, such as placental abruption, thereby avoiding an unnecessary preterm delivery.

Two-dimensional (2D) US allows a real-time examination to find fractures at any angle, even if the fetus moves. 2D US signs of a fracture are the shorter bone length for gestational age and angulation of long bones (Fig. 5.4). The advantage is an easy comparison with contralateral bone. One drawback is the requirement of a certain amount of amniotic fluid volume around the fetus [54].



**Fig. 5.3** Fetal head ultrasound at 27 weeks of pregnancy. (a) 34 h after trauma: fetal intracranial findings largely unremarkable—transverse view at the level of the lateral ventricle. (b) 62 h after trauma: a large hyperechoic lesion

in the frontal lobe (\*) as well as findings consistent with a subdural hematoma (arrows). (Reproduced with permission from [49] under the CC BY 4.0)



**Fig. 5.4** At 34 weeks gestation, a short right femur with a length corresponding to a gestational age of 26 weeks (48.9 mm right femur, 66.3 mm left femur). Angulated right femoral shaft suggests a fracture. (Reproduced with permission from [58])

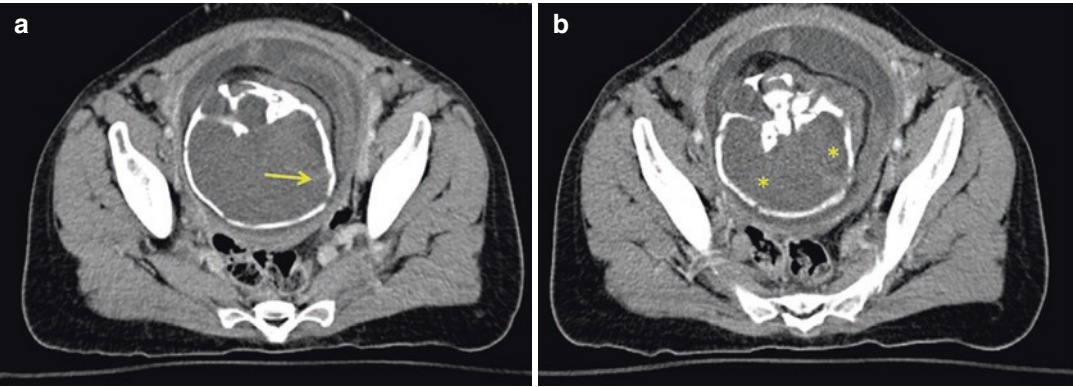
Diseases prone to intrauterine fractures should be evaluated. US signs of osteogenesis imperfecta type II can be detected from 13 weeks gestation—nuchal translucency, reduced echogenicity of the fetal bones, multiple fractures at various stages of healing, and deformity of the long bones, ribs, and skull [54]. Other types of osteogenesis imperfecta or skeletal dysplasia show bent but not broken bones detectable in the late second trimester [59, 60]. For the osteogenesis imperfecta, 3D US is more accurate in diag-

nosing all associated fetal fractures [54]. Doppler flow measurements of the umbilical artery may reveal high placental resistance associated with intrauterine growth retardation [61]. Oligo- or anhydramnios should raise a suspicion of placental insufficiency. All fetal organs should be examined and evaluated.

CT is not a primary imaging method for suspected fetal injuries except for the classification of maternal injuries. Fetal images are examined from the same CT scans [62–64].

During the third trimester, CT of the fetus identifies significantly more abnormalities than any US modality (CT 94.3%, 3D-US 77.1%, 2D-US, 51.4%,  $p < 0.01$ ) [54]. Another advantage of CT is 3D reconstruction, either as volume-rendering or in multiplane reformatting of the whole fetus or its segments (Fig. 5.5). The comparison of the diagnostic accuracy of different imaging methods for fetal skeletal issues is presented in Table 5.2.

Fetal MR is more accurate than the US for detecting axial skeleton anomalies or bent bones [65]. However, the emergent availability



**Fig. 5.5** Axial contrast-enhanced CT through the gravid uterus. (a) Deformation of the fetal skull (*arrow*). (b) Acute subarachnoid hemorrhages of the temporal and parietal lobes (\*). (Reproduced with permission from [64])

**Table 5.2** Diagnostic accuracy of different imaging methods for fetal skeletal regions

| Region/technique | 2D ultrasound | 3D ultrasound | Fetal CT |
|------------------|---------------|---------------|----------|
| Cranium          | (−)           | (++)          | (++)     |
| Face             | (−)           | (+)           | (++)     |
| Vertebrae        | (−)           | (+)           | (++)     |
| Ribs             | (−)           | (+)           | (++)     |
| Scapula          | (−−)          | (−)           | (++)     |
| Pelvis           | (−−)          | (−)           | (++)     |
| Metaphyses       | (++)          | (+)           | (++)     |
| Epiphyses        | (++)          | (+)           | (−)      |
| Extremities      | (++)          | (+)           | (−)      |
| Mineralization   | (−−)          | (−)           | (−)      |

Reproduced with permission from [66]  
*CT* computed tomography. (−−): very difficult; (−): difficult and/or does not visualize well; (+): easy and/or visualizes well; (++): visualizes very well

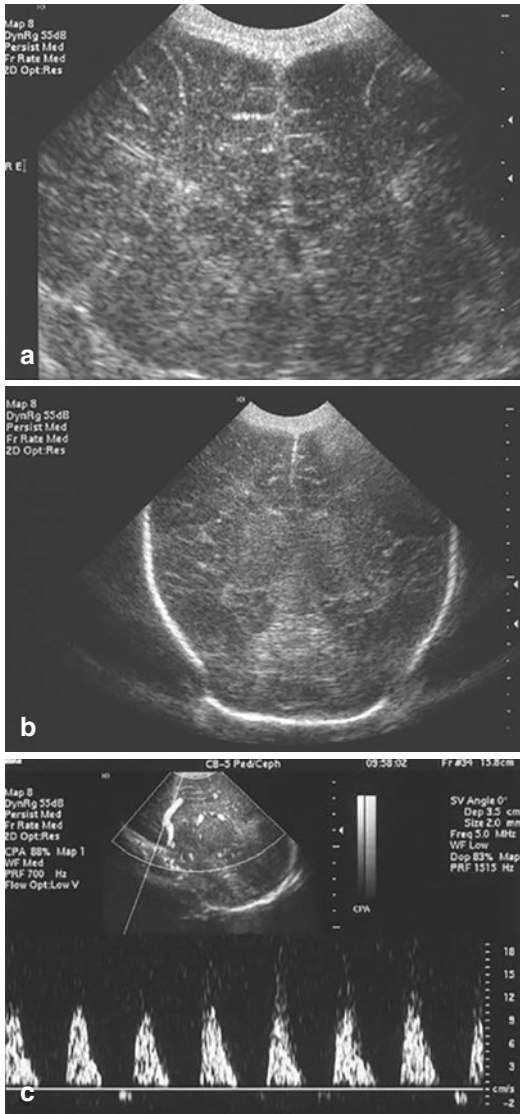
of MR and experts in fetal MR is still limited. The relatively long imaging acquisition times cause image degradation from fetal movement. Ultrafast MRI can overcome this disadvantage.

When a woman presents in pregnancy with a history of trauma, a Doppler US of the fetal and umbilical circulation over 48 h following the accident might allow recognition of hemodynamic disturbances. Serial fetal cerebral US or MRI of the brain soon after birth would detect the ischemic lesions, thus facilitating the timing of such prenatal cerebral insults.

**5.2.4.2 Postdelivery**

Injury of the fetus in blunt trauma is most frequent in the last trimester of pregnancy and often involves the fetal head [67, 68]. When emergent CS is indicated due to fetal distress, especially in the third trimester, and the newborn present with low Apgar scores, cranial (Doppler) US is mandatory. Doppler US of the major cerebral arteries defines the hemodynamic status of the brain, e.g., a high peak systolic and absence or inversion of the diastolic flow component on the flow curve suggest brain swelling (Fig. 5.6). More complex, especially





**Fig. 5.6** Cranial US, coronal and sagittal plane on the second day after emergent delivery at 37 weeks of gestation. (a, b) Cerebral edema: diffusely hypoechoogenic brain parenchyma, decreased visibility of the sulci and hazy delineation of the anatomic lines, slit-like ventricles; (c) the absent or reversed diastolic flow component suggesting increased vascular resistance in brain edema is demonstrated with spectral Doppler imaging. (Reproduced with permission from [67])

in the near-term infant, is a US evaluation of the pericerebral and pericerebellar spaces and smaller intraparenchymatous lesions, espe-

cially at the brain convexity and the fossa posterior. These lesions and skull fractures are evaluated in more detail with CT or MRI (Figs. 5.7 and 5.8).

#### 5.2.4.3 Diagnosis at Delivery

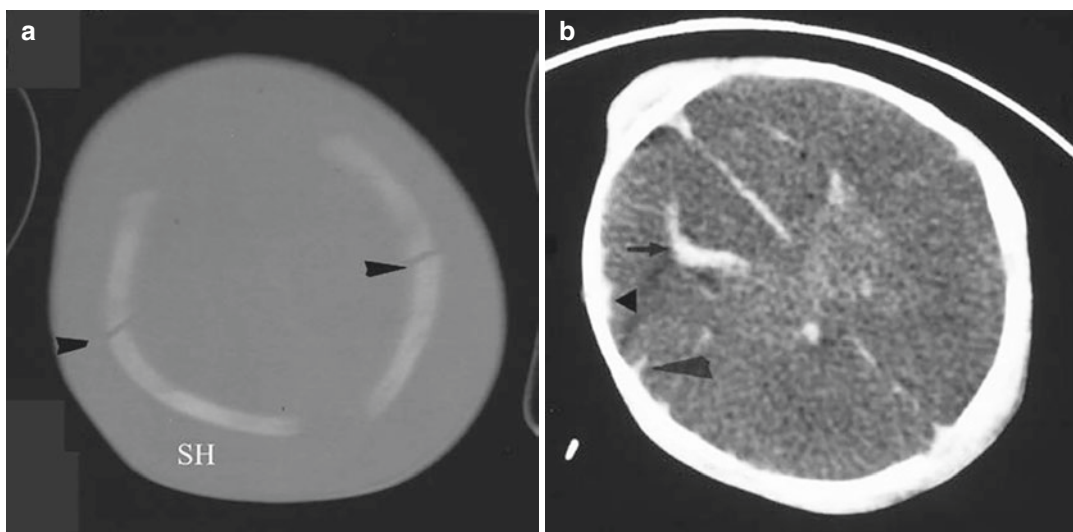
Diagnostic principles after delivery match those for neonatal trauma, birth trauma, or abnormal findings during a clinical examination. Difficult delivery is most commonly the result of a breech presentation. A “crack” is an essential sign for the early detection of a childbirth fracture [69] after vaginal delivery or CS. Birth-related fractures are fresh (Fig. 5.9), while intrauterine fractures delivered later show callus formation (Fig. 5.10). These fractures occur either with an underlying disease prone to fracture or from a difficult delivery. Underlying diseases should be excluded. These include osteogenesis imperfecta and other skeletal dysplasias, intrauterine growth retardation, prematurity, and osteoporosis.

In children with neurodevelopmental disorders of unknown etiology, a history of trauma in pregnancy should be sought, especially with neuroimaging features (MRI of the brain soon after birth showing the ischemic lesions) suggestive of a pre-term onset of injury [37].

#### 5.2.5 Differential Diagnosis

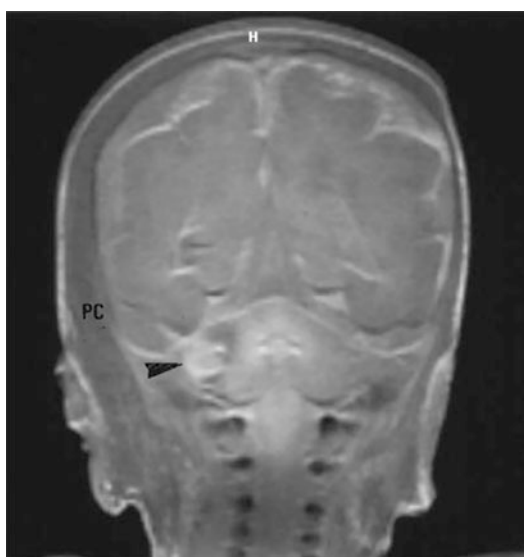
First, the etiology of the fracture should be defined. It can be spontaneous due to underlying fetal disease, maternal abdominal trauma, or a childbirth fracture (see Sect. 5.2.4.2). This is more important for the medicolegal issue than for differences in the treatment. The most common non-fracture differential diagnosis is congenital bone dysplasia found on X-ray (Fig. 5.11) or maternal transabdominal US (Fig. 5.12). The clinician should be aware of the possibility that even with maternal trauma, the fetus can have an underlying bone disease that should be excluded postnatally.





**Fig. 5.7** (a) Axial CT on the first day after emergency CS at 38 weeks of pregnancy. Subgaleal hematoma (*sh*) and bilateral parietal skull fracture (*arrowheads*). (b) Axial CT on the second day after emergency CS at 38 weeks of

pregnancy. Diffuse brain edema (hypodense parenchyma, hyperdense basal ganglia, no visible sulci), intraventricular (*arrow*), and subarachnoid hemorrhage (*arrowheads*). (Reproduced with permission from [67])



**Fig. 5.8** Postmortem coronal FLAIR MRI on the third day after emergency CS in 30 weeks' pregnancy. The extension (compared to previous ultrasound in Fig. 5.6) of the pericerebral hematoma (*pc*) and a cerebellar hemorrhagic (*arrowhead*) lesion. (Reproduced with permission from [67])



**Fig. 5.9** Elective lower segment transverse CS for breech presentation at 39 weeks' gestation resulted in a bilateral subtrochanteric fetal femoral fracture. (Reproduced with permission from [28])

### 5.2.6 Treatment

The timing and type of delivery depend on maternal status (see Sect. 25.3.8) and the type and estimated severity of the intrauterine fetal injury.



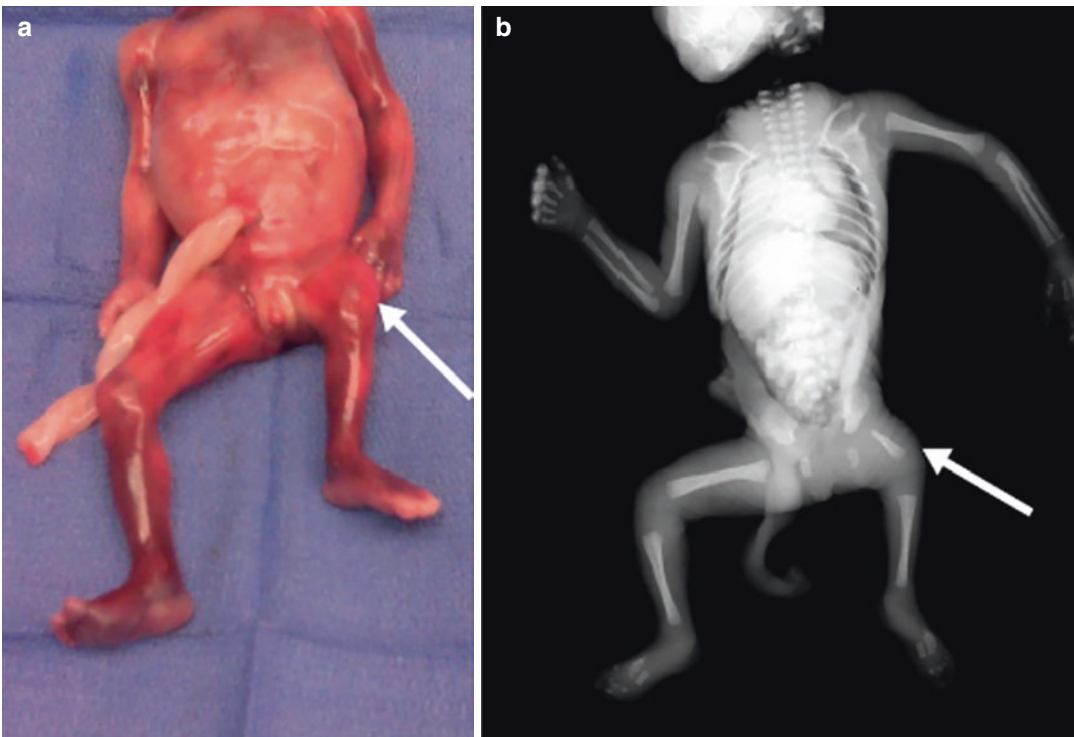
**Fig. 5.10** In addition to the callus, a minor lateral cortical defect at the apex of the angulation resembling a fracture was present on postdelivery plain X-ray. (Reproduced with permission from [58])

The timing and treatment type depends on the intrauterine fetal injury type and estimated severity.

#### 5.2.6.1 Intrauterine Fractures

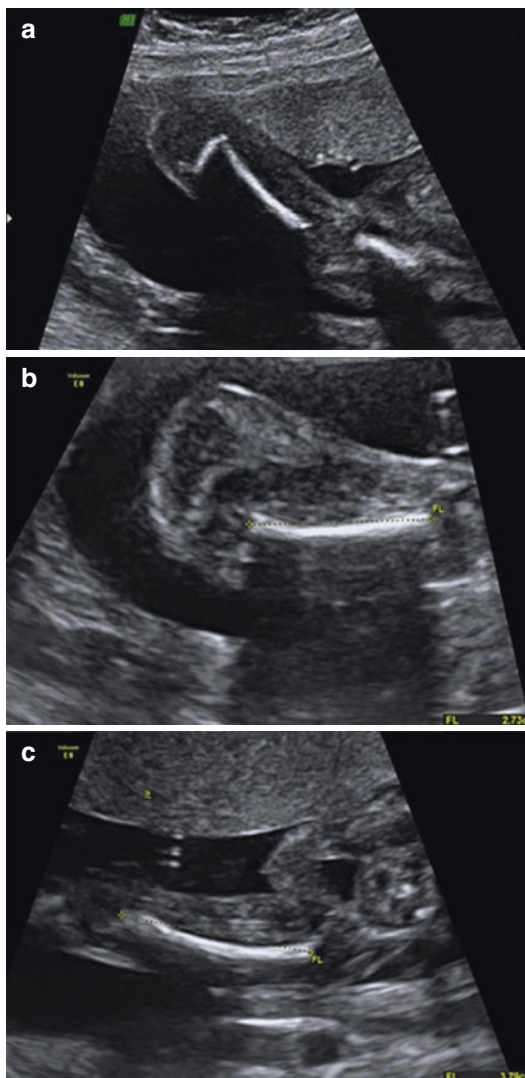
Uhde made one of the earliest reports on intrauterine fracture and healing in 1856 [72]. The maternal injury occurred in the seventh month of pregnancy. A term infant had fractures of the clavicle and humerus. The callus was at both fracture sites. Smith, in 1913, collected 44 cases of intrauterine fractures [73]. According to Page, Gurlt recorded 7 intrauterine fractures of the humerus and femur without interruption of pregnancy [74].

Intrauterine fractures may spontaneously heal in utero, as evidenced by callus formation at the fracture site [23]. Treatment of traumatic intrauterine fractures is primarily conservative. Nonnecrotic fetal long bone and fetal skull frac-



**Fig. 5.11** (a) Appearance of the fetus after the termination of pregnancy at 19 weeks' gestation showing a typical posture of congenital deficiency of the (short) femur (arrow). (b) A radiograph demonstrates unilateral short

femur (arrow) and acetabular dysplasia. The arrow in each figure part indicates a short femur. (Reproduced with permission from [70])



**Fig. 5.12** (a) Oblique view of the right femur misleads one to diagnose the intrauterine fracture. (b, c) Axial prenatal ultrasound image of the femurs shows that the right femur was markedly shorter than the left. The right femur measured 27.9 mm, three standard deviations below the mean for the gestational age. (Reproduced with permission from [71])

tures resolve spontaneously before birth [75, 76]. In mice, minimally displaced fractures during the second trimester unite within 48 h with little residual callus formation [77]. Prenatal healing is presumably enhanced by the attenuated intrauterine inflammatory response enhancing cell division [78] and possibly an angiogenic effect of the extraembryonic fetal stem cells

derived from amniotic fluid [79]. This benefit would diminish as the fetus approaches term due to (1) adult wound-healing mechanisms begin to develop [77], (2) more frequent and more pronounced fetal movements in advanced pregnancy [80], and (3) reduced amniotic space with more contact of fetal parts with the uterine wall during movements. In the 1990s, successful intrauterine open reduction and internal fixation of long bone fractures were demonstrated in an animal model [81–83]. There is no widespread use in human clinical practice. Intrauterine fetal operations are rarely indicated because even intrauterine fractures with angulation in a fetus without underlying disease result in spontaneous postnatal angulation correction during growth [84].

There are no guidelines for intrauterine fracture treatment in fetuses susceptible to fractures, as with osteogenesis imperfecta.

Fetuses with spontaneous intrauterine fractures without fetal distress should receive prenatal genetic testing for osteogenesis imperfecta by fetal US and amniocentesis or fetal blood sampling.

Prenatal transplantation of mesenchymal stem cells to treat fetal osteogenesis imperfecta was successful in two fetuses [85, 86]. This method could be applied as early after the diagnosis as possible for a better outcome.

### 5.2.6.2 Brain Injury

#### Subdural Hematoma

There are no indications for intrauterine treatment of SDH. In newborns, indications for the operation of posterior fossa SDH by Tanaka and Govaert [87] include (1) signs of brain-stem compression; (2) acute obstructive hydrocephalus with raised intracranial pressure; (3) a posterior fossa clot >15 cm, and (4) neurological deterioration. Observation is indicated in (1) small and non-expanding posterior fossa SDH, (2) acute convexity SDH, and (3) no neurological

deterioration [87]. Subdural taps are indicated with (1) increased intracranial pressure and (2) neurological deficits, indicating transtentorial herniation [87].

### 5.2.6.3 Birth-Related Fractures

(Bilateral) subtrochanteric fetal femoral fracture (Fig. 5.9) resulting from birth trauma is treated with immobilization in pelvipedal cast. Fracture healing is completed after 6 weeks [28].

Diaphyseal femur fractures are treated with a spica cast, the Pavlik harness, or Bryant skin traction [88]. Fractures treated with Bryant skin traction include both legs, with the hips flexed to 90°. Pulleys are attached to a specialized bed frame or improvised infusion stands with 100 mL bags of normal saline serving as weights (Fig. 5.13).

The weight should be such that the infant's buttocks are elevated 1 cm from the cot. Usually, up to 200 g is needed for each leg. A pediatric orthopedic surgeon should check the signs of vascular compromise or skin slough daily. Breastfeeding is not possible with the infants in the supine position in cots, and the mothers are encouraged to pump milk given to the babies. The babies with femoral fractures are kept in hospital and on traction until stability of the fracture (clinical and radiologic healing by 3 weeks with

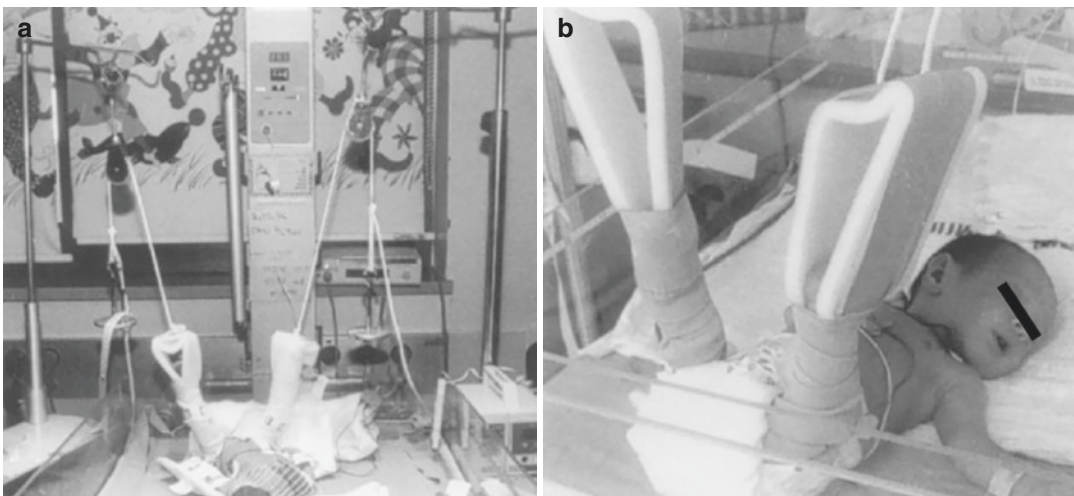
abundant callus formation). After release from traction, no further immobilization or splinting is needed. The long-term outcome (>5 years) is excellent, with no deformities, shortening, or other complications [27]. Discharging a baby in a Pavlik harness or any other fixation method requires close follow-up, increasing expenditure for frequent outpatient clinic visits, and specialized equipment.

### Cerebral Palsy

Hypoxic changes and encephalopathy could result from maternal hemorrhagic shock or direct fetal head trauma (see Sect. 4.7.3.1). Fetal head status can be evaluated with MRI during further pregnancy [89].

## 5.2.7 Prognosis

Trauma during the second and third trimesters has different clinical consequences than during the first trimester. Minor, first-trimester trauma does not threaten the pregnancy [90–92]. During the second and third trimesters, even minor trauma can have significant adverse effects on the fetus. Fetal loss can occur even when the mother has incurred no abdominal injuries [93, 94].



**Fig. 5.13** Baby with a fractured femur in Bryant traction. (a) Improvised use of infusion stands to hold traction weights. (b) Close-up of a child with both legs in Bryant

traction bed frame, with 100 mL bags of normal saline serving as weights. (Reproduced with permission from [27])



### 5.2.7.1 Fetal Mortality

The actual rate of spontaneous fetal loss in the general pregnant population is unknown. Estimates range is 10–15%, but with early spontaneous abortions, these values are 20–62% [95, 96]. However, a fetal loss of only 3% was reported [97, 98]. The fetal loss occurred in 4–61% of pregnant trauma patients, depending on the mechanism and severity of injury [93, 99–101]. Fetal death rate depends on the type of trauma: MVAs of 82–100% [102, 103], gunshot wounds of 6% [103], and falls of 3% [103], with maternal death accounting for 0–11% of the fetal deaths [102, 103]. Approximately 10–30% of pregnant women are exposed to significant physical abuse, with an associated 5% fetal death rate [93, 104–106]. Surgery for trauma has not been associated with an increased fetal loss rate [107].

In 1997 in the USA, it was estimated that 1,300–13,000 fetal deaths per year result from maternal MVA, and MVA was the leading cause of traumatic fetal death [108, 109]. In 2004, the trauma caused 13/100,000 fetal deaths in the USA [110]. The incidence of fetal death in maternal MVA is 4.7% [102]. Although some suggest that these estimates may be somewhat high, it seems clear that the number is significantly greater than the number of infant deaths caused by MVAs. It probably exceeds the total number of children aged 4 years and younger who died in MVAs [103, 111].

The issue of trauma as a true teratogen was raised. The US Environmental Protection Agency stated, “The introduction of nonhereditary birth defects in a developing fetus by exogenous factors such as physical or chemical agents acting in the womb to interfere with normal embryonic development”.

The most common causes of fetal death are direct injuries to the placenta, uterus, or fetus or maternal bleeding (with or without maternal death) [108]. Predictors of fetal death include the mechanism of injury and maternal and fetal factors (Table 5.3).

Emergency CS performed at >25 weeks of gestation with fetal heart rate following trauma carries 45% fetal survival [117].

**Table 5.3** Fetal mortality risk factors in trauma [25, 26, 94, 102, 108, 112–116]

| Mechanism of injury          | Maternal factors                       | Fetal factors             |
|------------------------------|----------------------------------------|---------------------------|
| Ejection from vehicle        | Maternal tachycardia                   | Abnormal fetal heart rate |
| Motorcycle collision         | Maternal hypotension                   |                           |
| Automobile-pedestrian injury | Maternal hypoxia                       |                           |
| Lack of restraints (3×)      | Maternal age <20 years                 |                           |
|                              | Maternal contractions                  |                           |
|                              | Injury severity score >9               |                           |
|                              | Pelvic fracture (48×)                  |                           |
|                              | Uterine rupture                        |                           |
|                              | Loss of consciousness (10×)            |                           |
|                              | Bicarbonate level at admission         |                           |
|                              | Disseminated intravascular coagulation |                           |
|                              | Placental abruption                    |                           |

Acetabulopelvic fracture carries a risk of fetal death of 35%. In contrast, acetabulopelvic fracture type (acetabular vs. pelvic) and fracture designation (simple vs. complex) do not influence maternal (see Sect. 25.3.3.5) and fetal mortality [118]. Whether the pelvic fracture itself directly adds to the poor fetal outcome or whether the pelvic fracture is a marker of significant transfer of kinetic energy to the fetus is difficult to discern. By some, most fetal deaths in this scenario are the result of spontaneous abortions without severe fetal trauma [102].

Although there have been dramatic improvements in the management and treatment of medical and obstetric conditions, fetal mortality, in general, has not been reduced because of a rise in nonobstetric causes (mostly MVAs). MVA in pregnancy is associated with a perinatal mortality rate of 3–6/100,000 live births in high-income countries, mainly attributable to placental abruption and uterine rupture [119]. The fetal/neonatal outcomes in the pregnancies delivered during the MVA admission, either spontaneously or in a

pregnancy complication such as placental abruption, were poor; one-third ended in perinatal death. Whereas some perinatal deaths are a result of spontaneous preterm birth, the high rate of CS (61.1%) in the group who delivered during the MVA admission suggests that a significant number underwent emergency delivery for maternal or fetal indications (e.g., placental abruption or abnormal fetal heart rate pattern on CTG). The low overall perinatal death rate of 1.4% during the admission immediately following an MVA in pregnancy  $\geq 20$  weeks is reassuring [90].

For women who did not require delivery during the MVA admission, the rate of pregnancy, delivery complications, and perinatal deaths is the same as for women without MVA during pregnancy [90].

In Saudi Arabia, fetal loss was higher in older, nonurban, employed women and women with family income  $>6,000$  Saudi riyals ( $>1,600$  US\$). It appears as a new prognostic factor, and higher family income could be a proxy for the presence of high-powered luxury cars, which may encourage fast driving [120].

The main causes of fetal death are placental abruption, maternal shock, and maternal death [26, 57, 93, 103, 112, 115, 117, 121].

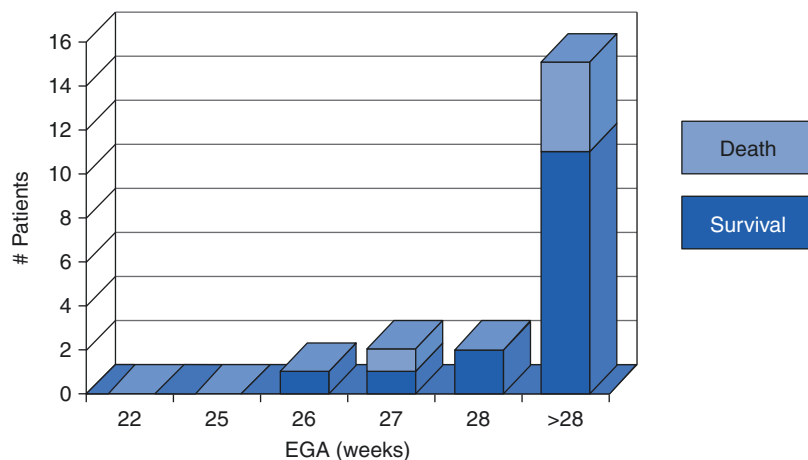
The rate of fetal death from maternal trauma was calculated to be 2.3/100,000 live births [103], while after major maternal blunt trauma it ranges 3.4–38.0% [25, 57, 93, 94, 99, 112, 113, 117, 122]. A maternal shock from major trauma has a 66–80% fetal mortality rate [101, 123]. Even nonsevere injuries (ISS  $<9$ ) carry significant maternal and fetal morbidity and mortality (Fig. 25.34) [124].

Placental abruption is the most common complication of blunt trauma in pregnancy [125] and is the leading cause of fetal death in 40–60% vs. 1–5% of nontraumatic causes of fetal death [126]. Until the 1970s, maternal death was the leading cause of fetal death [100].

Adverse pregnancy outcomes after minor trauma occur in 1–5% [127]. Because more than 90% of injuries to pregnant women result from minor trauma, most pregnancy losses occur after minor trauma [128]. Splenic and retroperitoneal injuries and hematomas are more frequent in pregnant patients with blunt abdominal trauma due to increased vascularity during pregnancy. Conversely, bowel injury is less frequent than in the general population [13, 14].

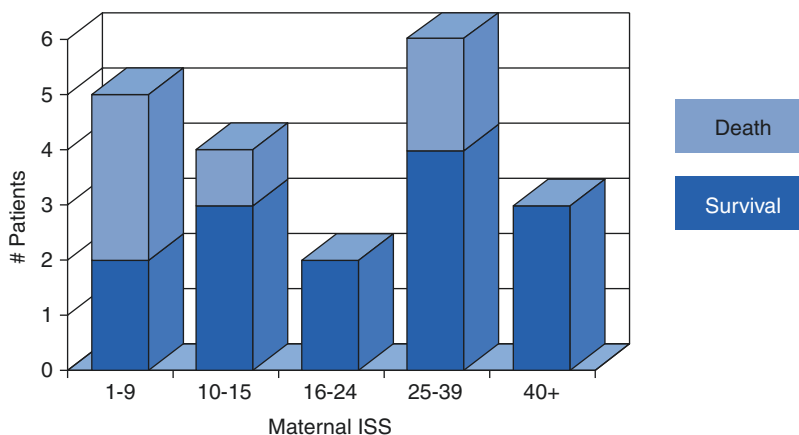
While some claim that gestational age is a strong predictor of fetal, neonatal, and infant death (Fig. 5.14) [124], others did not confirm it as a risk factor for fetal death [26, 102, 115]. ISS  $>2$  in the presence of a positive Kleihauer-Betke test result might effectively predict adverse fetal outcomes [129]. However, the value of ISS does not correlate with salvageable infant survival [47,

**Fig. 5.14** Salvageable infant survival, according to EGA. At EGA  $<26$  weeks, no infants survived. However, at EGA, between 26 and 28 weeks, the survival rate increases to 80%. EGA estimated gestational age. (Reproduced with permission from [117])





**Fig. 5.15** Salvageable infant survival, according to the maternal ISS. Infant death is distributed across the spectrum of severity, and even the most injured mothers have good infant survival. *ISS* injury severity score. (Reproduced with permission from [117])



[117] (Fig. 5.15). Fetal hemoglobin (HbF) assesses the risk for adverse perinatal outcomes identifying FMH. However, there may be no correlation between HbF and adverse fetal outcomes [130]. Maternal serum AFP >1,000 ng/mL predicts adverse fetal outcomes despite the minor maternal trauma and hemodynamic stability [130].

Maternal plasma bicarbonate level may be a predictor of outcome. Injured mothers with fetuses who survived had a mean plasma bicarbonate level of  $20.3 \pm 2.2$  mEq/L compared with  $16.4 \pm 3.0$  mEq/L in those with fetal loss [26].

Fetal head injury has a mortality rate of 43%, including intrauterine fetal demise and neonatal death [8]. However, 50% of survived children had good neurological outcomes [8]. Skull fractures with intracranial hemorrhage can cause death even without evidence of placental separation, uterine trauma, or maternal shock.

### Maternal Pelvic Fractures

In the third trimester of pregnancy, maternal pelvic trauma is a risk factor for direct fetal injury and mortality. Maternal pelvic fractures result in a fetal mortality rate of 13–67% [16, 25, 118, 131–133]. These studies did not consider possible additional intra-abdominal injuries that increase fetal mortality rate. With maternal intra-peritoneal hemorrhage, fetal mortality is 100%.

### Fetal Subdural Hematoma

The prognosis of fetal SDH depends on the severity of the bleeding and the underlying cause. The

mortality of spontaneous SDH is 57% [134]. Mortality of traumatic fetal SDH is lower than spontaneous—38% [8]. This is probably the result of earlier diagnostic workup due to maternal trauma and earlier delivery. Some CS of vital fetuses were concomitant with surgical exploration for maternal indications. In both groups, most newborns had some neurological impairment [134].

### 5.2.7.2 Fetal Morbidity

For comparing outcomes after fetal blunt and penetrating head injuries, see Sect. 5.3.6.1. Neurodevelopmental disorders are described in Sect. 4.7.3.

Spontaneous and traumatic femur fractures could result in shorter intrauterine and early post-natal femoral growth [29], or the femur and extremity growth are equal [135]. Long-term follow-up is lacking.

## 5.3 Penetrating Fetal Trauma

### 5.3.1 Incidence

Penetrating maternal abdominal trauma accounts for 9%, while blunt trauma accounts for 91% [92]. The first recorded case of a gunshot to the fetus appeared in 1845 [136], and stabbed fetus in 1930 [137]. The incidence of uterine gunshot wounds correlates to fetal gunshot wounds. The incidence of gunshot injury to the fetus probably

far exceeds the reported number of cases most of the time. Due to medicolegal issues, the family conceals the fact.

### 5.3.2 Pathophysiology

See Sect. 25.4.1.

#### 5.3.2.1 Fetal Gunshot Wound Characteristics

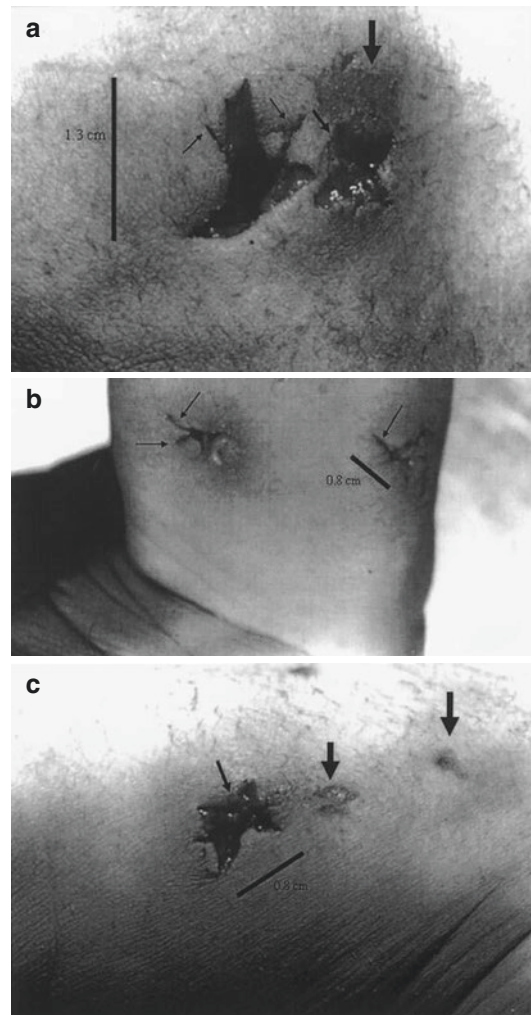
The fetal gunshot wounds do not have the characteristic features of entrance and exit gunshot wounds. Typical entrance gunshot wounds consist of circular perforations with marginal collars of abrasion, and typical exit gunshot wounds consist of slit-like to roughly circular perforations without margins of abrasion. The fetal gunshot wounds are atypical and do not demonstrate fire direction.

Catanese and Gilmore postulate that there are at least three factors that cause atypical gunshot wound characteristics in the fetus [138]:

- the presence of interposed tissues,
- shoring of the fetus against itself and the uterine walls,
- the composition and wound healing of fetal skin.

Bullets passing through interposed targets alter the ballistic stability of the projectile. An interposed target is any structure or material a bullet passes through before entering a body, including windows, cars, layers of clothing, or other persons. With a fetus injured by gunfire, the maternal body, the uterine walls, and the amniotic fluid serve as intermediate targets which can alter ballistic stability. After passing through an interposed target, a bullet will enter the second target with an altered trajectory, creating an atypical entrance wound. Also, the bullet can drag portions of the interposed target, such as pieces of bone or glass, along with it, which can further alter the entrance wound. Atypical injuries are known to occur due to the passage of projectiles through an interposed target [139].

At term, the proportion of fetal tissue to the amniotic fluid is increased, and many fetal body parts are in contact with each other and the uterus. Shored entrance and exit wounds occur when the skin through which a bullet enters or exits is pressed against a firm surface. When an exit wound is shored, the skin may show an irregular margin of abrasion as the elastic skin is stretched by the exiting bullet and rubbed against the shoring surface (Fig. 5.16). If an entrance wound is



**Fig. 5.16** Characteristics of fetal skin gunshot wounds. (a) Lacerations (*small arrow*), the margin of abrasion (*medium arrow*), adjacent abrasion (*large arrow*), (b) Arrows indicate lacerations; (c) adjacent abrasions (*large arrows*); lacerations (*small arrows*). (Reproduced with permission from [142])

shored, it is less likely to show a uniform margin of abrasion, and the injury pattern will depend on the nature of the surface in contact with the skin [140]. One example of a shored entrance wound occurs when a bullet perforates an extremity and then reenters the trunk or another body part. In such a case, the skin at the reentry site is in contact with the exit wound on the shoring extremity, commonly producing an irregular wound with an atypical margin of abrasion.

Fetal skin differs from the skin of an adult or even the skin of a child. The composition of fetal skin depends on the fetus's gestational age, as the morphogenesis of the appendages and the expression of the skin components is a sequential process. The fetal epidermis is covered by the periderm, an epithelial layer with many blebs and microvilli, creating a large surface area exposed to the fluid in the amniotic cavity. The periderm persists throughout gestation and modulates the interaction of fetal skin with amniotic fluid components, including steroids. Although it is unknown which cell receptors are used, it is known that steroids in the amniotic fluid affect both the water transport function and the types of keratin expressed in fetal skin. Fetal skin has a greater water content than adult skin [141]. More hydrated skin is softer with less resistance to a projectile. This could lessen the stretching caused by an entering or exiting projectile, causing an altered margin of abrasion or an atypical exit wound. At term, the collagens in the fetal skin are the same types that exist in adult skin, and they assume an adult configuration, but the relative amounts of collagen types differ. The predominant collagen in the adult skin is type I, thick, fibrous collagen. The predominant collagen in the fetal skin is type III, a fibrillary, interstitial type of collagen. In adults, type III collagen is restricted to the basement membranes and the perivascular areas [141]. This difference in collagen types may affect the skin's strength and resistance to the shearing forces caused by the velocity of a projectile.

### 5.3.2.2 Fetal Skin Restitution

It is very uncommon that maternal penetrating abdominal injury remains unnoticed without con-

sequences to the mother and fetus. Newborn or child injuries can become evident days, months, or even years after childbirth. The reason for maternal denial of trauma during pregnancy mainly includes medicolegal issues. For instance, it may be the result of a suicide attempt, which is a punishable crime in many countries, and when the death of the fetus occurs, this amounts to a culpable offense. Also, domestic violence is underreported.

If delivery occurs more than several weeks from the stabbing or gunshot wound to the fetus, skin scars could be invisible due to scarless fetal wound healing.

Scarring of fetal skin wounds begins at approximately 24 weeks of gestation [143].

The most important factor responsible for scarless healing is fetal fibroblast [143]. Embryonic wound healing shows a less differentiated inflammatory response. There is a change in the growth factor profile with low levels of  $TGF\beta_1$  and  $TGF\beta_2$  and platelet-derived growth factor with high levels of  $TGF\beta_3$ . Moreover, fibroblasts with increased synthetic capabilities deposit collagen rapidly and without scarring [144]. Other factors, such as fetal wound environment, different from adult tissue injury environment, like low  $pO_2$ , the absence of the polymorphonuclear leucocytes and immunoglobulins, and warm and sterile amniotic fluid could play a role.

Probably skin cell differentiation has a role in healing. At 3 weeks of gestation, the epidermis consists of a single layer of cuboidal cells developing from the embryonic ectoderm. By the 11th week, the epidermis has three distinctive layers: basal, intermediate, and superficial (periderm). Beneath the protective cover periderm, the epidermis stratifies and differentiates, forming the four distinct layers of the epidermis by the end of the fourth month of gestation. Periderm cells are replaced continuously until 21 weeks when it is completely shed and replaced by the stratum corneum.

### 5.3.3 Clinical Presentation

Most cases do not develop a clinical picture because emergent CS of vital fetuses is simultaneous with maternal exploration (see Sect. 5.3.5.1). Delivered fetuses should be examined, especially for stab wounds with small and undetectable entrance wounds (dagger, awl, etc.).

#### 5.3.3.1 Stab Wound

Most stab wounds are fresh because most fetuses are delivered at the time of the stabbing. In such cases, the edges of the fetal wound bleed (Fig. 5.17). If delivery occurs later, the skin wound morphology depends on the time interval between stabbing and delivery (see Sect. 5.3.2.2). Therefore, if there are scars on maternal abdominal skin, a delivered fetus should be checked for scars. Wounds should be examined for injuries of deeper structures along with neurocirculatory status. Sometimes injuries of deeper structures are evident (Fig. 5.18).

Fetal abdominal wound often results in intra-uterine bowel evisceration (Fig. 5.19).

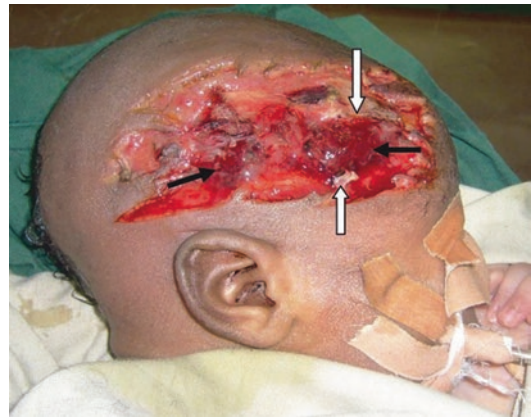


**Fig. 5.17** Fetal traumatic arrow wound on the face without intracranial injuries or neurologic deficit [145]

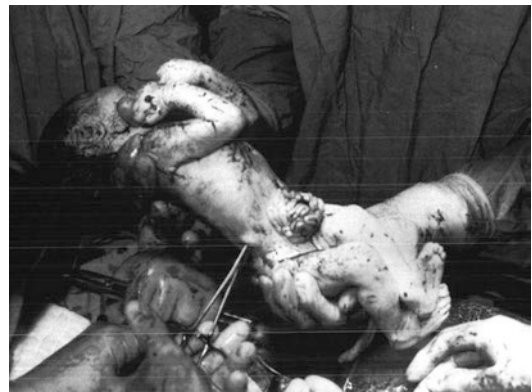
#### 5.3.3.2 Gunshot Wound

The fetal gunshot wounds have atypical features and do not demonstrate the direction of fire (see Sect. 5.3.2.1). Therefore, only if a single, superficial fetal wound and bullet outside the fetus are found, the cautious conclusion is that the wound is superficial without further surgical exploration of limbs and body cavities (Fig. 5.20a). On the contrary, diagnostic imaging is indicated if a single entrance wound is found without a projectile outside the fetus (Fig. 5.20b, c).

As in stab wounds, the time interval between shooting and delivery defines the skin wound



**Fig. 5.18** Compound brain injury with a wide, irregular scalp defect. Note hematoma over the brain surface (black arrows) and margins of the bony defect (white arrows). (Reproduced with permission from [146] under the CC BY 4.0)



**Fig. 5.19** A 1800 g stillborn with a right flank stab wound in continuity with the anterior abdominal wall wound through which bowel evisceration occurred. (Reproduced with permission from [147])





**Fig. 5.20** (a) Single or more superficial wounds on the same path with a bullet outside the body (*arrows*) do not mandate further surgical exploration. (Reproduced with permission from [148]), while (b) deep wounds. (Reproduced

with permission from [149]), and (c) entrance wound without exit wound and no projectile found necessitates diagnostic imaging and surgical exploration in most cases. (Reproduced with permission from [150] under the CC BY)



**Fig. 5.21** Newborn with superficial wound 8 cm long over the left scapula. The extremities of the wound healed, but its central portion was open for about 2.5 cm and was filled with healthy granulation tissue. No evidence of skeletal injury [151]

characteristics. Fresh wounds bleed while postponed delivery results in skin restitution, granulations, or wounds without bleeding (Fig. 5.21).

## Head

Survived cases are presented in Table 5.4.

### 5.3.3.3 Lethal Injuries

Stab or gunshot injuries that damage the vital structures are primarily incompatible with life.

Commonly, gross examination shows fatal injuries (Fig. 5.22). A high fetal mortality rate is partly due to the ratio of ‘volume of the injury’ and fetal volume. This is pronounced in the first half of pregnancy. Sometimes it is difficult to conclude whether maternal hypotension or fetal wound itself, especially a stab wound, is the cause of fetal death (Fig. 5.23).

### 5.3.3.4 Delayed Presentation

There are four types of delayed presentation: (1) asymptomatic, (2) deformations with or without lumps, (3) functional impairment, and (4) mental or cognitive impairment. With a penetrating wound at <24 weeks of gestational age, skin restitutes without scars. After delivery, no scars or skin marks can raise a suspicion of fetal injury (see Sect. 5.3.2.2).

Asymptomatic patients are diagnosed with retained metal parts, projectiles, or bullets when undergoing X-ray examination in later life for other indications. Only maternal medical history reveals penetrating maternal abdominal

**Table 5.4** Stab and gunshot wounds to the fetal head

| Stab wounds                |                                 |                                    |                            |                                                                        |                                                  |
|----------------------------|---------------------------------|------------------------------------|----------------------------|------------------------------------------------------------------------|--------------------------------------------------|
| Author                     | Gestational age                 | Delivery                           | Site of injury             | Neurologic status/deficit                                              | Treatment                                        |
| Badia et al. 1940          |                                 |                                    |                            |                                                                        |                                                  |
| Wright et al. 1953         |                                 |                                    |                            |                                                                        |                                                  |
| Shultz et al. 1993         |                                 |                                    |                            |                                                                        |                                                  |
| Avenarius 1997             | 29                              |                                    | Temporal                   | Intracerebral hemorrhage, subdural hematoma, hydrocephalus/hemiparesis | Evacuation of subdural hematoma                  |
| Gallo 2010 [152]           | 30                              | Spontaneous vaginal at 40 weeks    | Temporal                   | No deficit, presentation 3 years after delivery                        | Duroplasty, cranioplasty                         |
| Shehu et al. 2010 [146]    | Term                            | Traumatic CS at the time of injury | Frontoparietal             | Lacerated dura, no deficit                                             | Wound closure                                    |
| Parua 2015 [145]           | 36                              | Emergent CS at the time of injury  | Right cheek                | No                                                                     | No                                               |
| Gunshot wounds             |                                 |                                    |                            |                                                                        |                                                  |
| Author                     | Gestational age                 | Delivery                           | Site of injury             | Neurologic status/deficit                                              | Treatment                                        |
| Buchsbaum and Caruso 1969  | 36                              | Emergent CS at the time of injury  | Nasolabial                 | Superficial facial wound, no deficit                                   | No                                               |
| Edner et al. 1988 [153]    | 32                              | Emergent CS at time of injury      | Frontotemporal to parietal | Liquor leakage, no deficit                                             | Bullet removal at 9 months                       |
| Muzumdar et al. 2006 [158] | Term, postdelivery presentation | Spontaneous vaginal                | Parietal                   | Seizures, cerebritis, brain abscess                                    | Craniotomy, debridement                          |
| Gündoğmuş et al. [154]     | Term, postdelivery presentation | Elective CS after injury           | Unknown                    | Difficult speaking, no sphincter control, inferior motor tests         | Unknown                                          |
| Pham et al. 2018 [168]     | 38                              | Emergent CS at time of injury      | Temporal                   | Intraventricular hemorrhage, hydrocephalus, seizures, hemiparesis      | VP shunt at 5 weeks, bullet removal at 13 months |
| Gündoğmuş et al.           |                                 |                                    |                            |                                                                        |                                                  |

CS Cesarean section, VP ventriculoperitoneal shunt

trauma with normal fetal growth, delivery, and child development. No vital structures or structures that can cause neurovascular deficit were injured.

Deformations or lumps are mostly unnoticeable in the newborn. With neonatal development, these deformations can become more prominent (Fig. 5.24). Maternal medical history is essential. Otherwise, the diagnostic algorithm leads in the wrong direction to congenital diseases or tumors.

Like deformations, functional impairment can be evident earlier or later, depending on many factors. Asymmetric limb movements during the first postnatal life, asymmetric postures or limping, recurrent infections or sinuses from the same location, or recurrent organ infections could result from fetal penetrating injury, especially with retained nonbiologic objects/parts.

Although exceedingly rare, mental/cognitive child impairment could be due to nonvital fetal





**Fig. 5.22** The lethal penetrating hole in the fetal face and an exit hole in the fetal thorax. (Reproduced from [155] under the CC Attribution License). Entry and exit wounds on the uterus of the same patients are presented in Fig. 25.44

brain injury without external marks of intrauterine fetal head injury. It is commonly the result of severe head injury detected at emergent CS.

### 5.3.4 Diagnosis

Fetal injuries due to maternal penetrating abdominal trauma are diagnosed (1) preoperatively, when there is an indication for maternal diagnostic imaging with findings of potential fetal injuries or with abnormal CTG findings, (2) during maternal abdominal exploration for maternal injuries with confirmed uterine injury, (3) clinically, immediately after delivery, and (4) with delayed newborn or child presentation.

#### 5.3.4.1 Preoperative Diagnosis

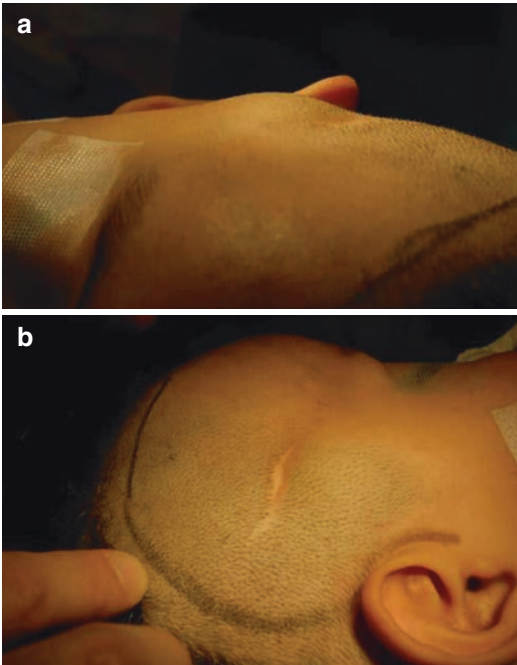
Two scenarios for the diagnosis of preoperative fetal injuries exist. First, fetal injuries can be expected with CTG signs of fetal distress without an indication for maternal abdominal exploration. Second, fetal injuries can be detected on maternal imaging diagnostics on plain X-rays, transabdominal US [153], or abdominal CT. Imaging preoperative fetal injuries is more challenging with stabbing because there are fewer fetal deformations and less possibility of retained foreign bodies visible on diagnostic imaging.



**Fig. 5.23** Fatal penetrating stab wound to the lower thorax in a pale fetus. The wound is similar to the one in Fig. 5.22. Sometimes, it is difficult to conclude whether maternal hypotension of fetal injury is the cause of fetal death. A fetal autopsy is not described. (Reproduced with permission from [156] under the CC BY 4.0 Attribution License)

#### 5.3.4.2 Intraoperative Diagnosis

Most fetal injuries are detected during the exploration of maternal intra-abdominal wounds, such as an abdominal gunshot wound, and most stab wounds indicate maternal abdominal exploration. A uterine wound carries a high probability of fetal injury, and CS should be considered in a viable fetus (see Sect. 25.4.4).



**Fig. 5.24** The first presentation of a 3-year-old child. (a) The bulging on the skin in the right temporal region; (b) A thin skin scar in the right temporal region [152]

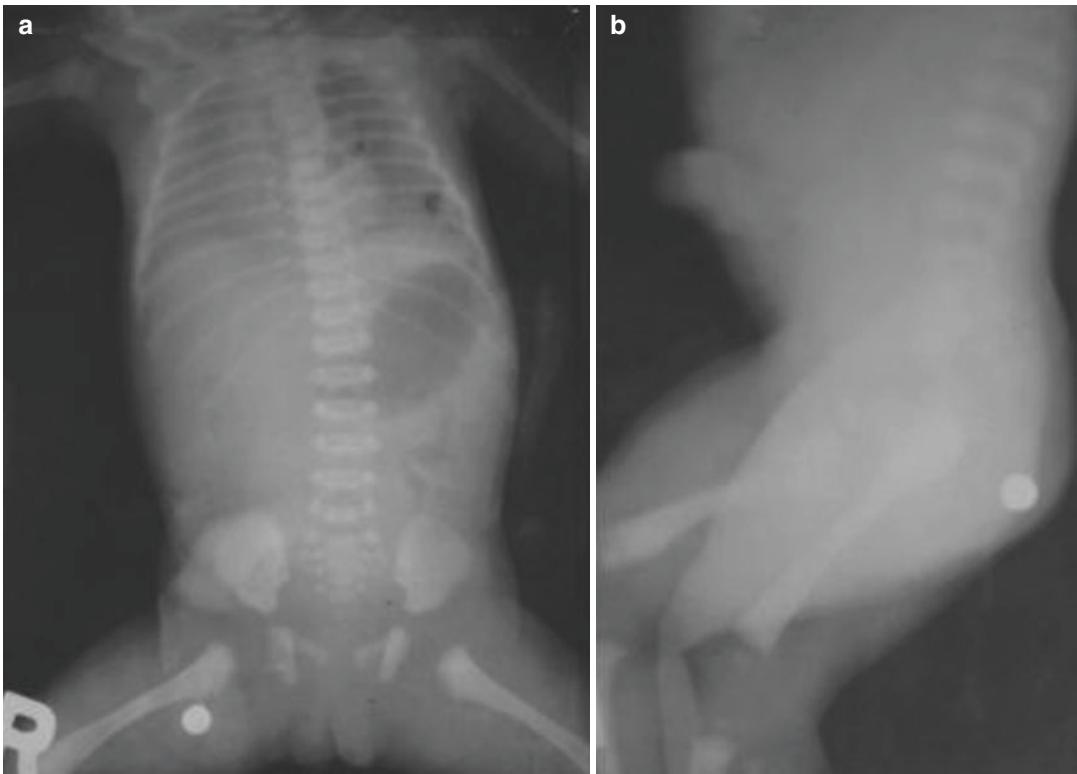
#### 5.3.4.3 Postdelivery Diagnosis

Even if the wounds seem superficial, primarily if projectiles are not found, focused plain X-rays, or babygram can show retained metal parts/bullets (Fig. 5.25) in the fetus [157] or fractures from projectile energy transmission. Therefore, a plain X-ray is recommended for gunshot wounds. For head injuries, brain US or head CT defines the extent of bleeding and retained foreign bodies [153, 158].

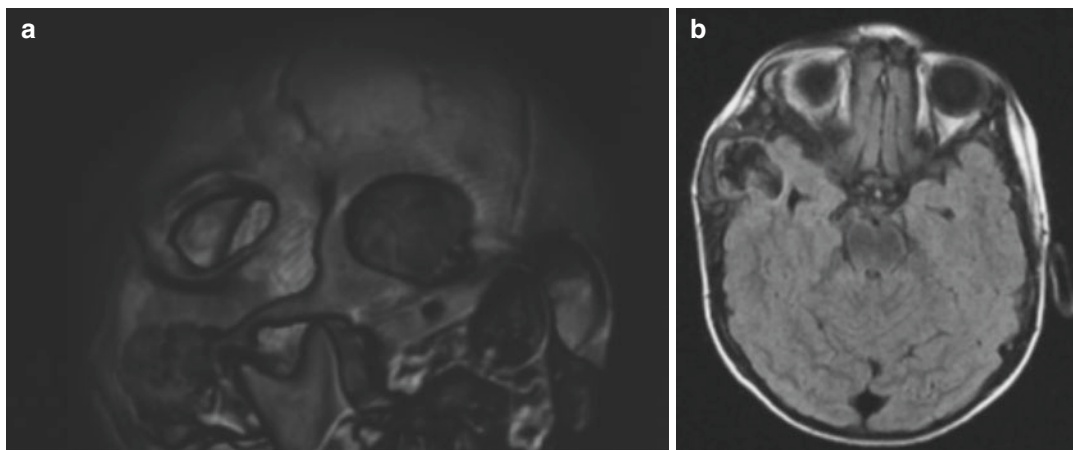
#### 5.3.4.4 Delayed Diagnosis

Delayed presentation, even after many years, can be noted as progressive deformities or enlarging lumps caused by retained foreign bodies [159], bony (Fig. 5.26), or internal defects as in the form of diaphragmatic hernia [160]. Also, fetal neurologic impairment should raise suspicion of a post-traumatic cause from intrauterine fetal injury [154].

Metal bodies are seen on plain X-rays (Fig. 5.27). As in blunt trauma, a specific condition is *growing skull fracture*. Growing skull

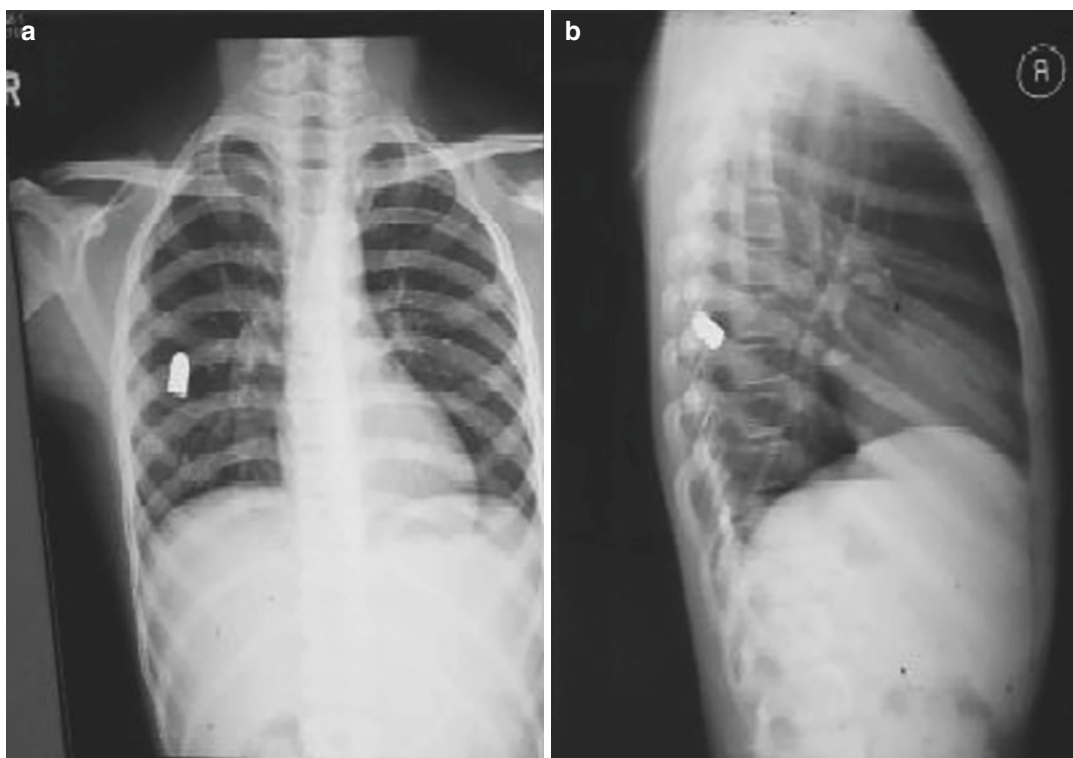


**Fig. 5.25** (a) Frontal and (b) lateral, plain abdominal X-rays of the abdomen showing the radiopaque bullet in the right thigh. (Reproduced with permission from [150] under the CC BY)



**Fig. 5.26** A 2.5-year-old abandoned child with a pulsating bulge in the right temporal region. Knife stab wound to the maternal abdomen at 30 weeks of pregnancy. (a) A 3D CT scan reveals a large right temporal bone defect; (b)

MRI showing herniation of the cicatricial cerebral tissue through the skull defect and a mild “blow out” of the homolateral temporal ventricular horn [152]



**Fig. 5.27** Chest X-ray (posteroanterior and right lateral) revealing radiopaque shadow (bullet) in a 10-year-old boy without signs of a postnatal gunshot injury. There were no

scars on the skin. (Reproduced with permission from [159] under the CC Attribution License)

fracture requires severe head injury to result in a skull fracture, a tear in the dura mater, or brain injury. The outward driving force, such as a normally growing brain, is the mechanism underlying the formation of the growing fracture [161]. These elements explain why most growing fractures occur in very young children or intrauterine fetal head injuries [152].

### 5.3.5 Treatment

#### 5.3.5.1 Obstetric Management

With a live fetus, risks of prematurity must be weighed against the benefits of delivery for and treatment of the suspected fetal injury. Indications for emergent CS in an alive and viable fetus are:

- radiologic signs of penetrating head injury or visible intracranial foreign bodies,
- radiologic signs of thoracoabdominal injury or visible intracranial foreign bodies,
- CTG abnormalities.

#### 5.3.5.2 General Wound Treatment

Due to a small number of cases, there are no firm recommendations for specific penetrating fetal injuries.

Principles of stab or gunshot wound to the delivered viable fetus should follow neonatal and pediatric surgery principles.

Since infants have been born alive with soft tissue and visceral injuries, the hazards of prematurity must be weighed against the potential benefits of operation to the injured premature infant delivered by CS. When fetal weight approaches 2,500 g, these hazards are greatly diminished.

#### Tetanus Vaccinations/Prophylaxis

For maternal prophylaxis, see Sect. 25.4.4.1. To avoid generalized neonatal tetanus, maternal vaccination during the last trimester (not earlier) of pregnancy induces intrauterine active fetal immunization [162]. This is due to the fetal immune sys-

tem's progressive maturation and the placenta's increased permeability during the last months of pregnancy. Vaccine effectiveness of  $\geq 2$  properly timed doses of tetanus toxoid given to pregnant women against neonatal tetanus mortality is 94% [163]. Transplacental immunization circumvents the necessity for immunization in early neonatal life (up to 13 months) [164]. Guidelines about vaccination or prophylaxis for emergent CS shortly after immunization do not exist. There is no evidence of adverse fetal effects from vaccinating pregnant women with an inactivated virus, bacterial vaccine, or toxoid. A growing body of robust data demonstrates the safety of such use [165].

#### Prophylactic Antibiotics

In most cases, antibiotics are not even mentioned. As in nonpregnant population broad-spectrum antibiotics, FDA class B, eventually, class C should be administered to the mother. With the continuation of pregnancy, transplacental antibiotic transfer protects a fetus. There are no recommendations on fetal antibiotic prophylaxis if emergent CS is performed at the time of injury.

#### 5.3.5.3 Subcutaneous and Limb Injury

Tangential skin injuries resulting from stab and gunshot wounds (Fig. 5.20a) need only debridement and dressings. For the deeper penetration into the limbs (Figs. 5.20b and 5.28) with the



**Fig. 5.28** Bullet entrance hole in a fetus treated conservatively. Post-injury plain X-ray did not reveal metal parts, but the newborn was lost in follow-up. (Reproduced with permission from [166])



possibility of injury of important structures (nerves, blood vessels, bones, tendons, joints), no clear guidelines exist [166]. However, exploration is recommended except in puncture wounds without signs of compartment or significant edema. The neurovascular deficit is an absolute indication for exploration. The radiologic examination is necessary to define retained metal parts with only the entrance wound on limbs.

### 5.3.5.4 Head Injury

#### Neuroprotection

One of the unsolved issues is post-traumatic neuroprotection. Many potential targets for neuroprotection—antagonists of the NMDA receptors for glutamate, magnesium sulfate, and tianeptine block the effects of inflammatory cytokines, NSAIDs, and growth factors—are effective in animals and in vitro experiments. However, there is no firm data on humans [167].

#### Brain Surgery

Several authors recommend postponed removal of projectiles when the newborn does not show (1) significant neurologic deficits, (2) intracranial bleeding, (3) increased intracranial pressure, or (4) infective complications mandating exploration [153, 168]. Repeated US or CT examinations should be used to monitor fetal course noninvasively. The possible adverse effect could be lead poisoning with the potential of a child's failure to thrive [169]. Some authors claim it is only present when the bullet is included in the circulating fluids like synovial [170] or cerebrospinal [171, 172]. If any of the conditions above are present, immediate exploration is mandatory [158].

In stable newborns with noncomplicated penetrating intracranial injury, when all issues related to prematurity are solved, the idea to postpone the operation at around 1 year of age minimizes the risk of further brain injury, with a potential of lead poisoning. The infant's age for safe projectile removal depends on the localization of the projectile and the infant's condition.

### 5.3.5.5 Thoracoabdominal Injury

In hemodynamically unstable fetuses, surgical exploration is mandatory.

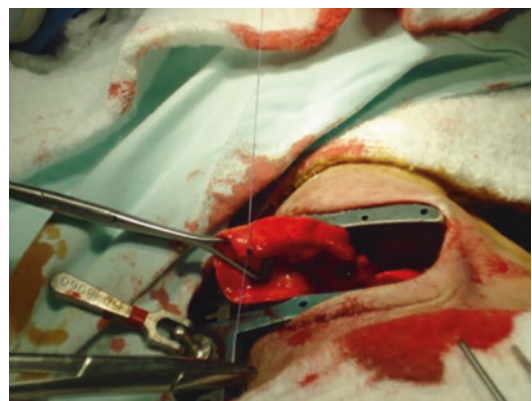
In the stable fetus, gunshot wounds to the thorax or abdomen indicate thoracotomy or laparotomy, while stab wounds could be managed nonoperatively. Peripheral thoracic gunshot wounds could be treated with a chest tube. The risk of delayed complications includes a diaphragmatic hernia [160]. Wound exploration is mandatory [173]. Further exploration is recommended with the pleural or peritoneal injury due to a high possibility of organ injury when the dagger to fetal body ratio is considered [174]. Further procedures depend on the injury type and principles that follow pediatric surgery principles (closure of pleural, peritoneal, diaphragmatic, bowel injuries/defects, and bleeding control) (Fig. 5.29).

Absorbable sutures are used to repair minor lacerations in the lungs or bowel (Fig. 5.29).

After bowel resections or simple sutures, breastfeeding can start on postoperative day 2 if the newborn is stabilized without mechanical ventilation [174].

### 5.3.6 Prognosis

The fetus has a worse prognosis than the mother, with an injury rate of 59–80% and a perinatal mortality rate of 40–71% [92, 175, 176]. The



**Fig. 5.29** Lung laceration from the gunshot wound repaired with primary suture. (Reproduced with permission from [174] under the CC BY Attribution License)

perinatal mortality during 1957–1967 was 71% [23], unchanged from 1845–1964 [177]. After 1967, there was a decrease to 59% [23]. From 1845 to 1954, fetal mortality of viable fetuses was 55% [178]. In the same period, the fetal mortality among those with vaginal deliveries was 66%; among those who had abdominal deliveries, 46%. Perinatal mortality of viable fetuses up to 1972 was 59% [179].

Fetal trauma after stabbing injuries to the uterine cavity occurred in approximately 50%, with fetal survival of 80% [180–182]. All parts of the fetal body are equally affected.

Factors that have an impact on fetal outcome are (1) fetal factors, in addition to (2) maternal factors (placental injury, placental abruption, disseminated intravascular coagulation, and maternal hypovolemia), and (3) availability of tertiary centers for high-risk neonates. Fetal factors that have an impact on fetal outcome are:

- the second trimester of pregnancy,
- multiple > single wounds,
- gunshot > stabbing wounds,
- thoracoabdominal wounds.

Pregnancy loss was significantly greater in women in the second trimester than in the first trimester. The second trimester represents the most vulnerable period for all types of fetal trauma because the gravid uterus ascends out of the bony pelvis in the cephalad direction to reach the level of the umbilicus by 24 weeks; here, the gravid uterus may sustain a direct traumatic injury. In the third trimester, the fetus is well protected by the thickened uterine wall and the amniotic fluid [120]. However, in both gunshot and stab wounds, the fetus presents a larger target as the pregnancy progresses and is more likely to sustain an injury [14, 183–186].

Fetal morbidity depends on the gestational age, location, and extent of injured structures and organs. However, functional impairment is mostly lesser [160, 173], except for head injuries (see 5.3.6.1), than in children and adults.

With gunshot wounds, fetal injuries range from 60 to 90%, and overall perinatal mortality is up to 70% [14, 179, 184, 187]. A significant portion of fetal death in stabbing and gunshot wounds is due to immaturity from ill-timed delivery. Until 1977, fetal mortality was 78% if intrauterine gunshot wounding occurred preterm, but only 40% for injuries at term [188].

Several decades ago, after stabbing injuries to the uterine cavity, fetal trauma occurred in 93%, with fetal mortality of 47% [186]. Recent fetal mortality decreased to 27.3% [180].

### 5.3.6.1 Penetrating Head Injury

Intrauterine penetrating fetal head injury has a high mortality [158]. With maternal abdominal stab wounds, the fetal head is injured in 10% of cases [152]. Many survived newborns have neurologic deficiencies. The incidence and the extent of neurologic deficit depend on the factors listed in the following tables (Tables 5.4 and 5.5):

As for fetal mortality, gunshot wounds carry a much higher rate of a post-injury neurologic deficit than fetal head stab injuries. Despite attenuation from the uterine wall and amniotic fluid, projectiles from explosive weapons transmit more energy to the surrounding tissues. An additional consequence is a higher risk of surrounding necrosis and infective complications necessitating further conservative and surgical therapy, mainly debridement, and abscess drainage. In cases of fetal cerebral ischemia, reperfusion injury also contributes to brain damage. Prematurity and preterm delivery could also contribute to neurocognitive development [153]. Also, additional general anesthesia in neonates

**Table 5.5** Factors contributing to the neurologic deficit after fetal penetrating head injuries

| Related to head injury                  | Unrelated to head injury            |
|-----------------------------------------|-------------------------------------|
| Type of wound/weapon                    | Maternal hemorrhage or septic shock |
| Extent of primary brain damage          | Fetal hemorrhage/hypoxia            |
| Severity of primary brain damage        | Socioeconomic factors               |
| Secondary brain damage                  | Prematurity                         |
| Number of operations/general anesthesia | Lead toxicity                       |



contributes to cognitive impairment. Maternal hemorrhagic or septic shock also contributes to worse outcome, primarily if associated with placental abruption, placental tear, or disseminated intravascular coagulation. Retroplacental bleeding can lead to feto-maternal transfusion, fetal anemia, hypovolemia, and hypoxia (see Sect. 25.3.6).

The degree and dynamics of neurologic deficiencies are challenging for prognosis due to a small number of patients. However, all survived fetuses developed hydrocephalus, seizures, and intellectual or cognitive disabilities. Children <5 years at the time of injury had more intellectual impairment than children with similar injuries later. Socioeconomic factors are also important. Long-term functional therapy influences long-term neurodevelopmental outcomes as for any other type of injury, while it is of utmost importance for a head injury.

### 5.3.6.2 Penetrating Thoracoabdominal Injury

Fetal thoracoabdominal gunshot wounds 40 years ago had a mortality rate of  $\approx 100\%$  [188, 189], while current mortality is 50% [156].

### 5.3.6.3 Perimortem Cesarean Section

The outcome of postmortem CS for all causes was poor until recently. In the German duchy Kurhessen in 1848, there were 107 cases with no survivors [190]. In 1864, in 147 cases at the Berlin Obstetrical Society, only three infants survived [191]. Katz et al. reviewed the literature from 1879 through 1985 and reported 269 cases with 188 infant survivors with probable underreporting of unsuccessful cases [190]. Katz et al. associated infant survival with the time interval between maternal death and delivery. In their review of cases from 1900 to 1985, there were 61 cases with neonatal survival and known time intervals. Fifty-seven (93%) were born within 15 min, and only two had neurological damage, one mild and one severe. Seventy percent of the survivors were born within 5 min [190]. There are cases with live infants with postmortem CS between 7 and 22 min after documented maternal cardiac arrest. Follow-up of infants demonstrated

no evidence of neurologic damage [191, 192]. Strong et al., in 1989, reported that about half of the perimortem CS in the literature had produced live infants. However, the incidence of neurological sequel increases with increasing delays to delivery. The long-term survival rate for healthy infants was 15% [193].

Of infants delivered by this method in general, approximately 15% survive and are discharged from the hospital in good condition [194–196]. The survival of these infants depends on how soon they are extracted, their maturity, the duration and nature of the mother's illness, the performance of postmortem maternal CPR, and the availability of neonatal intensive care [197]. Although recent reviews conclude that despite reports of 30 years supporting perimortem CS, they fail to prove that it improves maternal and neonatal outcomes [198]. Of the 330 reported cases of postmortem CS during the eighteenth century, only 7 living children recovered. Then, in 1916, fetal survival of 42.3% was published [199].

If the mother is stabilized, but the extent of maternal injuries precludes maternal salvage, there is another option except for perimortem CS. Improved life support for premature infants and their mothers who sustained fatal injury increased the possibility of successful pregnancy outcomes. This is primarily applicable for maternal injury resulting in brain death. Mother is maintained on life support systems until the fetus reaches maturity [200].

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## Part II

# Gynecology

### Abstract

Adnexal torsion is one of the most common nonobstetric gynecologic, acute abdominal conditions in pregnancy. Due to the growing uterus, adnexa are pushed from the pelvic to an abdominal position making them more prone to torsion. With the widespread use of assisted reproductive technologies resulting in ovarian hyperstimulation syndrome, adnexal torsion is even more common. Due to the often nonspecific clinical presentation, differential diagnosis is wide with some side-specific differential diagnoses. Sonography has high diagnostic sensitivity and specificity, and abdominal MRI is used in uncertain cases. Its use is increasing because it accurately distinguishes acute appendicitis from adnexal torsion. The treatment is operative with increased use of nonresectional procedures. If malignancy is not suspected or proved, an additional reason for early operative detorsion is ovarian salvage in early pregnancy, which hormonal role is essential for the normal progression of pregnancy.

## 6.1 Introduction

*When a pregnant woman has violent diarrhea, there is a danger of her miscarrying in a pregnant woman if the breasts suddenly lose their fullness, she has a miscarriage.*

*If in a woman pregnant with twins, either of her breasts lose its fullness, she will part with one of her children; and if it is the right breast which becomes slender, it will be the male child, or if the left, the female.*

*When women, in a moderate condition of the body, miscarry in the second or third month, without any obvious cause, their cotyledons are filled with mucosity, and cannot support the weight of the fetus, but are broken asunder.*

*In women that are about to miscarry, the breasts become slender; but if again they become hard, there will be a pain, either in the breasts, or in the hip-joints, or the eyes, or in the knees, and they will not miscarry.*

*Women with a child who are seized with fevers, and who are greatly emaciated, without any (other?) obvious cause, have difficult and dangerous labors, and if they miscarry, they are in danger.*

(Hippocrates, 400 BC).

Evaluation of a patient during pregnancy with acute abdominal pain should always include a search for surgical and gynecologic disorders. Parsons, in 1958, stated that 40% of women in the general population who present with symptoms of pain in the lower abdomen and pelvis do not have the gynecologic disease [1].

Preservation of reproductive capability (child-bearing, hormonal function, and sexual health) impacts a woman's wellness. This critical issue should be considered in the surgical management of acute gynecologic problems.

*Adnexa* is the anatomical area adjacent to the uterus and contains the fallopian tube, ovary, associated vessels, ligaments, and connective tissue. *Adnexal torsion* (AT) is a total or partial rota-

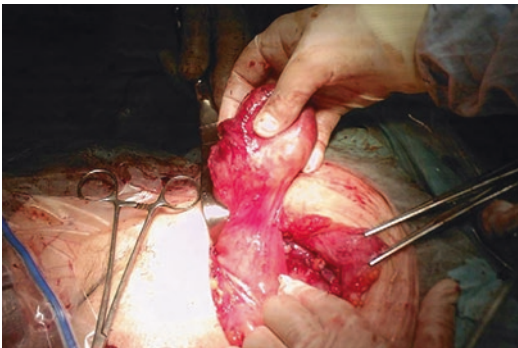
tion of the adnexa around its vascular pedicle resulting in ischemia.

## 6.2 Historical Perspective

Morgagni first described AT in 1748 and Rokitansky in 1850. Kuestner, in 1891, first described an ovarian torsion (OT) in a nonpregnant female [2]. Hartmann, in 1898, first described AT in pregnancy [3], then Pinard in 1901 [4], Nicholson J. Eastman (President of American College of Obstetricians and Gynecologists, (1961–62) in 1927 [5], Green-Armytage in 1929 [6], and Sheldon in 1936 [7]. In 1909, Gifford Nash published a case of isolated torsion of paraovarian cyst during early pregnancy [8], and Fleming, in 1920, published an ovarian cyst in the fifth month of pregnancy [9], both without AT. Due to the adherence and the size of the ovarian cyst, Fleming resected the involved left Fallopian tube.

## 6.3 Incidence

The prevalence is probably underestimated primarily due to spontaneous detorsion [10, 11] or ovarian autoamputation without other symptoms or complications (Fig. 6.1). Surgical treatment of AT constitutes 2.7% of all gynecological emergent surgeries during pregnancy [12]. The preva-



**Fig. 6.1** Macroscopic appearance of incidentally found autoamputated ovary in the cul-de-sac during Cesarean section for the lack of labor progress. (Reproduced with permission from [17])

lence of AT is 1–5/10,000 spontaneous pregnancies [12, 13]. Isolated OT has reported an incidence of 1–10/10,000 spontaneous pregnancies [14–16].

Torsion of hydatids of Morgagni involving the ipsilateral Fallopian tube causes acute abdominal pain in adolescents; AT constitutes approximately 25%. However, the condition is uncommon in adult females [18], representing a marginal part of ATs, rarely during pregnancy (see Chap. 7).

However, AT has been reported in 7–28% of all pregnancies complicated by adnexal masses [19–24]. AT is an essential concern of pregnancy-associated adnexal masses and had a much higher incidence (13.8%) than malignancy (3.4%) [25]. The reported incidence of adnexal tumor torsion varies widely, ranging from 0.8% [26] to 53.8% of tumors undergoing antepartum surgery [27].

In an 80-year review, Jubb collected only 34 cases of ovarian cancer during pregnancy [28]. In 1973, Munnell emphasized the infrequent association between ovarian cancer and pregnancy at 1/18,000 pregnancies [29]. More recent comprehensive reports summarized the incidence of 0.18–2.8/10,000 pregnancies [30, 31]. It is uncertain whether the incidence of ovarian cancer associated with pregnancy rises. However, since the childbearing age among older women increases, cancer incidence is also likely to rise during pregnancy. In one study, 98% were elective cases with only one emergent operation for AT [32]. Bilateral torsion is infrequent, simultaneously or sequentially, with few cases reported [33, 34].

An incidence of AT with adnexal mass decreases as the gestational age increases [14, 33, 35]. In contrast, torsion of the normal adnexa during pregnancy or the postpartum period is extremely rare, without known incidence.

## 6.4 Risk Factors

### 6.4.1 Adnexal Mass

Depending on the method and definition of a clinically significant adnexal mass, the prevalence of pregnancies complicated by an adnexal mass is 1–8% [36–39]. Approximately 5% of

these represent malignant tumors, making ovarian cancer the fifth most common cancer diagnosed during pregnancy (see Chap. 8) [40]. The incidence of simple or complex ovarian cysts in pregnancy is 5–8%, of which 0.7–3.8% undergo torsion [39, 41, 42]. Table 8.1 lists adnexal masses unique to pregnancy, while Table 8.2 shows the incidence of histopathologically confirmed ovarian tumors during pregnancy. The most common tumor in pregnancy is benign cystic teratoma (22–40% of all ovarian tumors) [43]. Therefore, it is the most common tumor found with AT. Torsion occurs in 19% and ruptures in 17% of mature cystic teratomas in pregnancy

**Table 6.1** Pathological findings of ovarian torsion in pregnant women

| Pathological finding <sup>a</sup> | (%) |
|-----------------------------------|-----|
| Teratoma                          | 30  |
| Corpus luteum cyst                | 20  |
| Follicular cyst                   | 15  |
| Serous cystadenoma                | 15  |
| Endometrioma                      | 10  |
| Mucinous cystadenoma              | 5   |

Reproduced with permission from [68]

<sup>a</sup>Two cases undergoing detorsion were without pathological results

**Table 6.2** Differential diagnosis of right-sided and left-sided adnexal torsion (side differences in *italic*)

| Right-sided                                | Left-sided                            |
|--------------------------------------------|---------------------------------------|
| Renal colic                                | Renal colic                           |
| Renal or urethral calculi/obstruction      | Renal or urethral calculi/obstruction |
| Ectopic/heterotopic pregnancy              | Ectopic/heterotopic pregnancy         |
| Hemorrhagic/corpus luteum cysts            | Hemorrhagic/corpus luteum cysts       |
| Pyosalpinx/hydrosalpinx                    | Pyosalpinx/hydrosalpinx               |
| Pelvic inflammatory disease                | Pelvic inflammatory disease           |
| Ovarian hyperstimulation syndrome          | Ovarian hyperstimulation syndrome     |
| Nonpregnant horn of bicornuate uterus      | Nonpregnant horn of bicornuate uterus |
| Bowel obstruction/perforation              | Bowel obstruction/perforation         |
| <i>Periappendicular abscess/infiltrate</i> | <i>Sigmoid diverticulitis/abscess</i> |
| <i>Meckel's diverticulitis</i>             |                                       |
| <i>Ileocolic Crohn's disease</i>           |                                       |
| <i>Ovarian vein thrombosis</i>             |                                       |

[44]. Complete torsion causes a venous and lymphatic blockage, leading to stasis, venous congestion, hemorrhage, and necrosis. The cyst/tumor becomes tense and may rupture. Whether the type of tumor has a predilection for isolated tumor torsion or AT in pregnancy is unknown.

Adnexal masses of 6–8 cm have a higher risk of adnexal torsion [25].

An explanation could be that a larger ovarian mass hardly goes into a torsion due to the mass effect. AT before the tenth week and after the 20th week of gestation had a tumor 6–8 cm. However, tumors with larger diameters could undergo AT within the tenth and 17th week of gestation, likely because the adnexal tumor had been carried out of the pelvic cavity by the gravid uterus and had a larger surrounding environment. After the 20th week, the incidence of AT declines [25].

## 6.4.2 Anatomic Variations of Adnexa

The torsion of normal ovaries is due to hypermobile ovarian ligaments, long ovarian ligaments, or other inherent ovarian mobility. Other mechanisms include abrupt changes in intra-abdominal pressure with vomiting and coughing, adnexal venous congestion during pregnancy, and sudden acceleration/deceleration movements [45–47]. The location changes of the adnexa and the uterus (i.e., the ovaries emerging from the pelvis by the increasing size of the uterus) may predispose the ovaries to twist by allowing them greater mobility [48]. The main histopathologic findings are follicular or corpus luteum cysts [49].

## 6.4.3 Assisted Reproductive Technologies

The increased use of assisted reproductive technologies (ART), such as controlled ovarian hyperstimulation, in vitro fertilization (IVF), and

intracytoplasmic sperm injection, increase the risk of AT, particularly when ovarian hyperstimulation syndrome (OHSS) develops. The increased risk of AT with OHSS is due to the bilaterally enlarged ovaries with multiple follicular or lutein cysts in hyperstimulated patients, especially in those who become pregnant with persistent cysts. There is no side predilection [50]. Even bilateral AT was described [50, 51].

OHSS is the risk factor in 50% of twin pregnancies from ART [52].

The incidence of AT with OHSS in nonpregnant is 2.3% and 16% in pregnant women [26]. However, 12–25% of all AT occurs in pregnant women, often combined with ART and its complications. The incidence is low for oocyte donation cycles (0–0.2%) and IVF cycles (0–0.13%). However, the incidence increases to 6% with stimulation for ART and to 16% with OHSS [13, 26, 42, 53–57]. However, even when AT occurs simultaneously with OHSS, the incidence varies between 1 and 33% [33]. Seventy percent of torsions occur in multiple pregnancies [53, 54, 58]. The incidence of fresh embryo transfer is 0.35% [59]. There are cases with OHSS treated successfully, but patients developed AT in the more advanced pregnancy [53]. The proportion of patients with a twin pregnancy and ART in the <28 weeks group was significantly higher than that in the ≥28 weeks group [60].

#### 6.4.4 Pregnancy and Trimester

Pregnancy is a risk factor for (recurrent) AT or isolated OT without ovarian mass, despite the method of conception and gestational age at the time of torsion. Recurrent torsion is more frequent in multicystic ovaries [14, 35]. The risk of OT rises by five times during pregnancy [25], and prevalence decreases in late pregnancy [13], as well as isolated OT [14, 15]. Ectopic pregnancy can also be found on the contralateral side, presenting with AT [61].

Most ATs occur in the first (by some 70% [62]) or second trimester of pregnancy, with 5.9–10% in the third trimester [13, 25, 26, 45, 59, 63–66]. Conception by ART is prone to first trimester AT [62]. The puerperal patient is more prone to AT because of the rapid anatomic changes in the pelvis, accompanied by the involution of the uterus. At the same time, the utero-ovarian ligament remains disproportionately stretched, allowing the normal-sized ovary increased space to move and twist. This is most common during the first postpartum week [47, 67], although it can occur after 3 weeks postpartum [25]. Probably the women start to move, bend, and lift more. Sudden movement/rotation is a risk factor for AT.

The gravid uterus generally experiences dextrorotation, and 80% of AT in pregnancy are right-sided [59, 62].

No significant differences between <28 weeks group and ≥28 weeks group in terms of the size of the adnexal mass, the cycles of AT, and the duration from onset to operation exist [61].

## 6.5 Pathology

It is important to define the pathologic cause of AT. Table 6.1 shows the pathology of adnexal masses causing torsion in pregnancy. If the mass is benign, there is no need for additional surgical or oncologic therapy.

## 6.6 Clinical Presentation

### 6.6.1 Medical History

The presenting complaint of AT is abdominal pain, in more than 80% of patients, abrupt in nature, very severe, in the right or left lower abdominal quadrant, with no relieving factors, including analgesics [52, 69–71]. It is often described as sharp and “knifelike,” although it



can be colicky and persists for 24 h [26, 72, 73]. Abdominal pain is usually followed by nausea and vomiting [52]. The pain is proportional to the degree of circulatory obstruction; complete obstruction interrupting venous return results in sudden severe pain with nausea and vomiting developing rapidly. In addition to abdominal pain, flank pain is commonly present [54, 67], and the pain may radiate to the back or groin. There may be a history of waxing and waning pain if the adnexa has been twisting and untwisting or has undergone partial torsion, causing vascular slowdown but not thrombosis [26, 57, 74]. The infundibulopelvic ligament may twist and untwist by itself, reducing and increasing the pain. There may be a history of some jarring or movement that has caused the torsion, such as exercise before the onset of the pain or even just turning over in bed. Patients could have adnexal masses diagnosed before or even during pregnancy. Commonly, there is no history of vaginal bleeding or discharge, diarrhea, constipation, fever, or urinary complaints [52, 71].

### 6.6.2 Physical Examination

Signs of peritoneal irritation, considered fundamental for the diagnosis, are present in 43% of pregnant women and 19% of nonpregnant women [14, 33, 75]. Pelvic examination usually reveals a tender mass on the affected side. If the patient had normal adnexa before the torsion, she might not have a mass present until later in the torsion when edema and swelling of the adnexa have set in. Therefore, serial examinations may be necessary for a patient suspected of AT. The pain is usually lower with a twisted ovarian cyst than with acute appendicitis. It is more continuous and followed early by a mass that rapidly increases in size. Patients rarely have evidence of abdominal guarding or rebound tenderness on physical examination. Patients are mostly afebrile [52, 54]. A low-grade fever may occur [71], but significant fevers point to another cause of pain. Tachycardia with normal blood pressure, pulse, and temperature indicate a noninflammatory condition [76]. The extent of bleeding depends on

the degree and duration of torsion. Hemorrhagic infarction occurs later but never with a large amount of hemoperitoneum. Bimanual examination defines mass felt through the fornix separately from the uterus. Tenderness is present, and mass is not moving with movements of the cervix. If not advanced pregnancy, the cervix is closed without signs of bleeding or discharge [71]. In advanced pregnancy, cervical dilation can be present. Uterine contraction or preterm labor, in addition to abdominal pain, is found in advanced pregnancy [52, 53].

## 6.7 Differential Diagnosis

AT should always be a differential diagnosis of acute pelvic/abdominal pain in women, especially those with pelvic masses diagnosed by examination or ultrasound (US). The differential diagnosis differs for right-sided and left-sided AT mostly due to surgical conditions (Table 6.2) [70, 73, 77]. Gynecologic/Obstetric and urologic differential diagnoses are the same for both sides. The differential diagnosis of AT is challenging in combination with OHSS, as abdominal pain, nausea, and vomiting are symptoms of hyperstimulation or pregnancy. The abdomen is already distended and tender because of the enlarged cystic ovaries [74]. Low-grade fever can accompany AT, but with high fever, inflammatory conditions such as tubo-ovarian abscess, pyosalpinx, or pelvic inflammatory disease (see Chap. 13) or non-obstetric inflammatory conditions should be suspected.

## 6.8 Diagnosis

### 6.8.1 Laboratory Findings

Serum leukocyte levels are commonly normal [71], especially in the early phase. Leukocytosis may be present [54] but is not predictive, primarily because of common physiologic leucocytosis of pregnancy [33, 72, 73]. In the general female population, it is present in 56% [69]. Leukocytosis may change with OHSS. If necrosis and infection of the twisted organ occur, then higher fever and

higher (or progression of) leukocytosis may be present.  $\beta$ HCG should be routinely checked in suspected or proven cases of AT because pregnancy is a risk factor for AT (see Sect. 6.4.4), especially if additional risk factors for ectopic pregnancy are present (see Chap. 9).

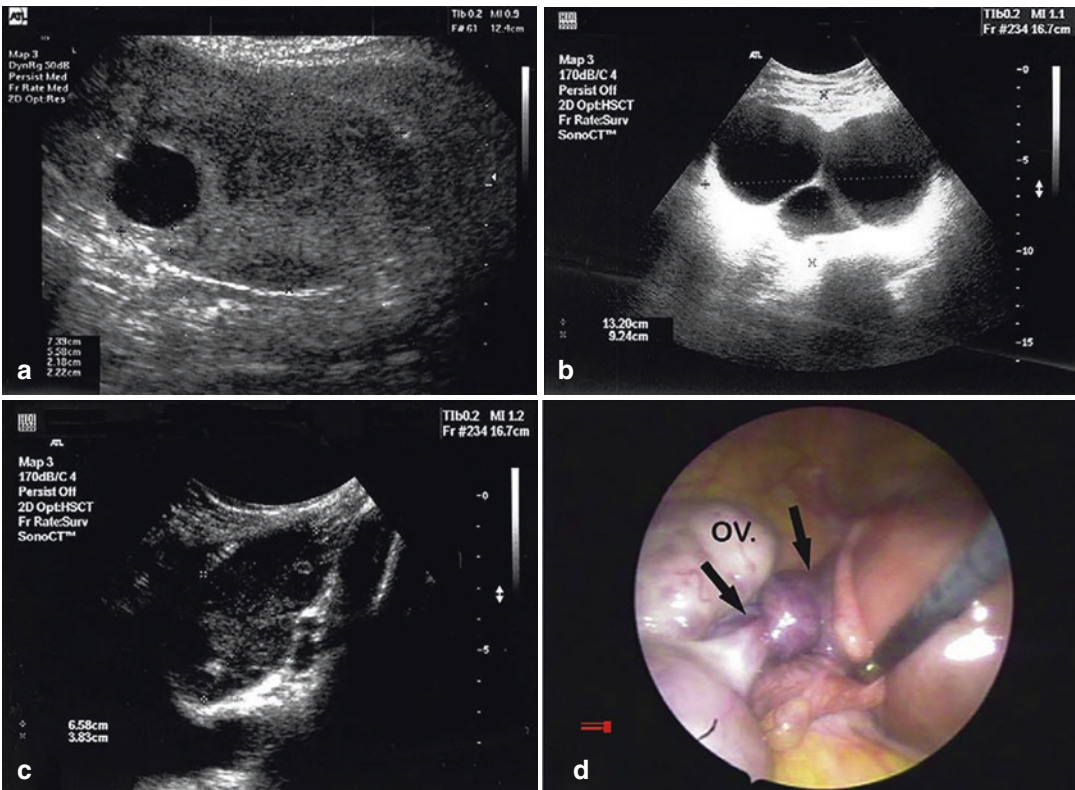
Hemoglobin/hematocrit is commonly normal [54, 71]. Physiologic anemia of pregnancy complicates the interpretation. With a AT lasting 12–24 h, a small decrease in values can be observed due to transudation of the blood-stained fluid or (hemorrhagic) cyst rupture [46] or hemorrhagic infarction. Urinalysis is normal [54].

### 6.8.2 Transvaginal Ultrasound

The transvaginal US often shows an enlargement of the ovaries and polycystic changes without this being evidence of torsion. It is extremely rare

for AT to occur with a mass <5 cm [59, 78]. Nonetheless, a large mass might sometimes be missed in the third-trimester presentations when a large uterus can hide the adnexa. The ovarian parenchyma is initially congested because of varying degrees of ovarian arterial, venous, and lymphatic occlusion with AT (Fig. 6.2), and hemorrhagic infarction occurs later [20, 79]. US findings associated with the diagnosis of AT include a predominantly solid-appearing ovary, unilateral ovarian enlargement, peripheral cystic structures, and marked stromal edema and pelvic fluid [57, 79–83].

OHSS presents a significant differential diagnostic problem. Twisted adnexa is usually characterized by a solid-appearing ovary on US, organ enlargement, ovarian peripheral cystic structures, and marked stromal edema and pelvic fluid. These characteristics are routinely present in a hyperstimulated ovary, and usually, both



**Fig. 6.2** Different ultrasound images of twisted ovaries in pregnancy. (a) A transabdominal scan of an enlarged ovary with a 20 mm simple unilocular cyst. The ovarian parenchyma appears edematous; (b) transabdominal scan of an enlarged 130 × 92 mm ovary with multicystic com-

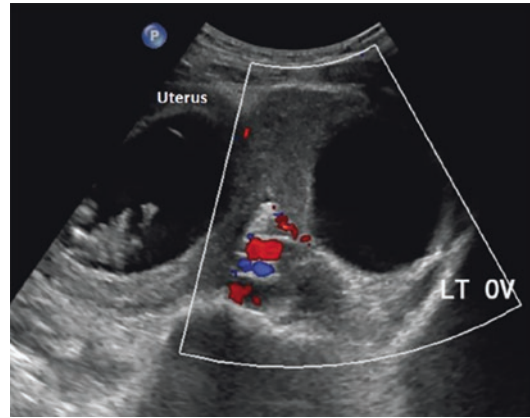
ponents; (c) transabdominal scan of an enlarged 65 mm ovary without cystic components. The ovarian parenchyma appears edematous; (d) laparoscopic view of torsion. Arrowheads point to the twisted ovarian pedicle. (Reproduced with permission from [48])

adnexa are enlarged. Mild OHSS could be suspected in these patients, delaying the correct diagnosis and treatment. There is an overlap in the grey-scale appearance of ovaries in mild OHSS and OT. Ovaries in mild OHSS are enlarged, with prominent, heterogeneous stroma, and contain multiple 1–2 cm follicles, many containing hemorrhages. Torsed ovaries are also enlarged, with prominent, heterogeneous central stroma and multiple, small peripheral follicles [84]. Also, in OHSS, both ovaries could be enlarged and symmetrical, contrary to the situation with AT [73].

Although the absence of Doppler flow (Fig. 6.3) has a high specificity for arterial occlusion and AT [54, 71], the presence of flow (Fig. 6.4) should not exclude AT (low sensitivity) [80–83, 85, 86]. This depends on the stage of the torsion and the degree of vascular compression. During the early stage of torsion, the venous and lymphatic obstruction starts. Arterial flow may only be decreased at this stage. Doppler US cor-



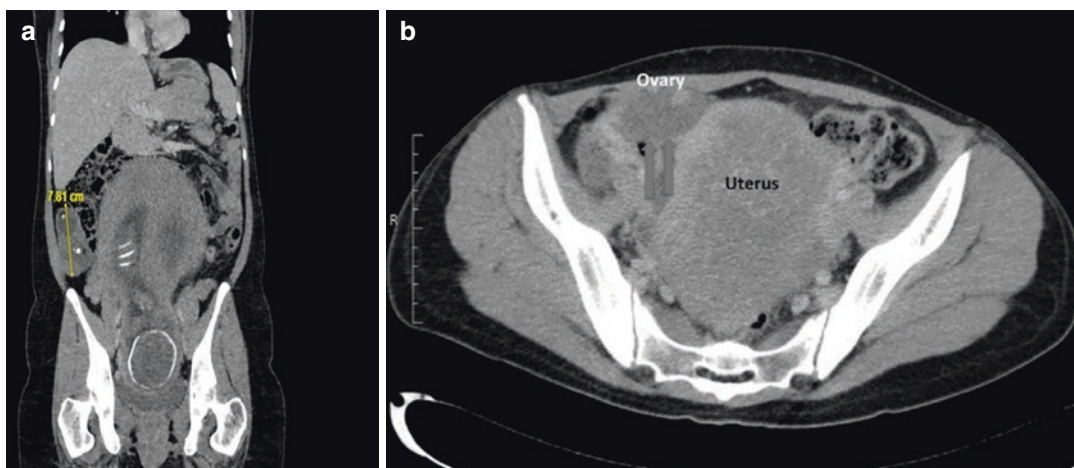
**Fig. 6.3** Doppler mapping of the left adnexa showing the absence of vascular flow. (Reproduced with permission from [85])



**Fig. 6.4** Doppler sonogram shows intrauterine pregnancy and left ovarian cyst with the flow to the ovary, intraoperatively found to be ovarian torsion. (Reproduced with permission from [76] under the CC Attribution License)

rectly diagnoses AT in the general female population in 40–60% of surgically confirmed cases [14, 86, 87]. With OHSS, ovaries often show an increase in diastolic blood flow; thus, decreased blood flow may indicate AT in patients with OHSS [86, 88]. Furthermore, the reduction in diastolic flow is diagnostic of OT in patients with OHSS. In the hyperstimulated ovary, the diastolic flow is usually increased [89]. However, a torsed ovary may demonstrate normal venous and arterial flow entirely symmetric for the normal side [84].

The decision for surgical evaluation should not rely only on the results of the Doppler flow investigation. It should also consider past medical history, clinical appearance, and laboratory assessment [14, 73]. Close monitoring is necessary to achieve timely management with a conservative approach.



**Fig. 6.5** (a) CT (coronal view) at 32 weeks of pregnancy shows calcifications of the right adnexal mass being ovarian teratoma [52]. (b) Postpartum right ovary slightly

enlarged and located anterior to the uterus. (Reproduced with permission from [47] under the CC BY 3.0)

### 6.8.3 Abdominal CT

Abdominal CT is rarely performed during pregnancy [52]. Most cases underwent a CT scan in puerperium [47]. Based on CT findings, the correct preoperative diagnosis of AT in a general female population is 34% [90]. The most common but nonspecific finding of OT is an enlarged ovary (Fig. 6.5) (>4 cm in maximal dimension) with or without a mass [47, 52].

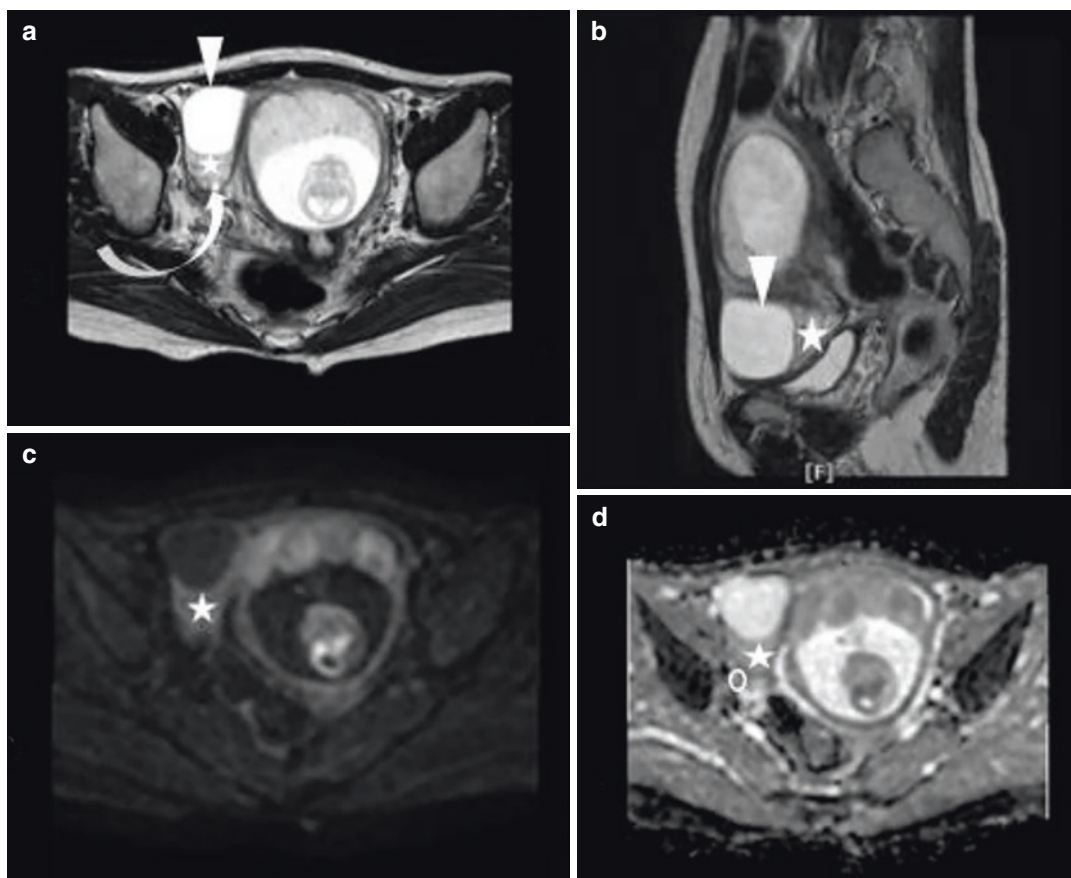
### 6.8.4 Abdominal MRI

MRI is useful in diagnosing OT in the second and third trimesters of pregnancy when the ovaries

are difficult to visualize on US [91]. Also, if the diagnosis cannot be established, especially in cases with OHSS, an emergent abdominopelvic MRI could define the AT. The MRI appearance of AT includes a hemorrhagic Fallopian tube. This twisted ovarian tumor can result in hemorrhagic infarction with the lack of enhancement in the multiple internal septa of the tumor [92]. Solid ovarian tissue appears enlarged and edematous (Fig. 6.6).

Currently, the diagnosis of AT is missed in 15–35% because of nonspecific clinical features and uncommon objective findings [24, 49, 68]. More frequent MRI use in doubtful cases could increase preoperative diagnostic accuracy.





**Fig. 6.6** Eight weeks of pregnancy with acute adnexal torsion without hemorrhagic infarction. (a) Transaxial T2-weighted single-shot turbo spin-echo MRI shows hyperintense swollen ovarian medullary stroma (*star*) and prominent cortical follicle (*curved arrow*) in the torsed enlarged right ovary. (b) 3.5 cm unilocular cystic mass (*arrowhead*) in the normal-appearing ovary was pathologically confirmed as a corpus luteal cyst. (c) Transaxial

diffusion-weighted MRI shows hyperintense swollen ovarian medullary stroma (*star*). (d) Apparent diffuse coefficient value indicating the region of interest of  $1.83 \pm 0.11 \times 10^{-3} \text{ mm}^2/\text{s}$  in the ovarian medulla (*star*) and  $1.57 \pm 0.14 \times 10^{-3} \text{ mm}^2$  in the ovarian cortex (*circle*), respectively. (Reproduced with permission from [93] CC Attribution 4.0 International (CC BY 4.0))

## 6.9 Treatment

Early diagnosis and prompt surgical intervention result in ovarian and adnexal preservation from infarction. In elective settings, because of the high incidence of adverse pregnancy outcomes associated with emergency surgery, some recommend elective removal of all non-acute masses that persist until 16 weeks or  $\geq 6$  cm regardless of appearance on imaging studies, unless it is suspected to be a leiomyoma [94].

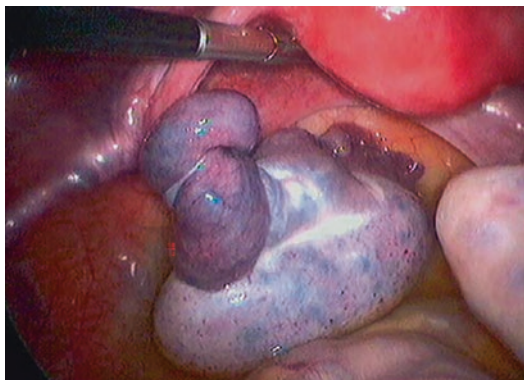
### 6.9.1 Operative Principles

*Laparoscopy is recommended for both diagnosis and treatment of adnexal torsion unless clinical severity warrants laparotomy.*

(SAGES guideline)

#### 6.9.1.1 Abdominal Access

Without classic symptoms and no definitive diagnostic tests or studies, surgical exploration of the pelvis provides a definitive diagnosis (Fig. 6.7). Laparoscopy has become the preferred surgical



**Fig. 6.7** Laparoscopic view of torsion of the enlarged left adnexa. (Reproduced with permission from [59])

approach for diagnosing and managing AT in pregnancy [95]. It results in shorter operative time and hospitalization, reduced narcotics consumption, minimized fetal exposure to analgetics, greater patient comfort, and lower discomfort of stretching and distension incisions and scars due to the rapidly growing uterus compared to laparotomy [12, 20, 23]. Therefore, abdominal wall dehiscence or herniation during labor rates is lower. A panoramic view of the pelvis reduces intraoperative uterine manipulation, decreasing postoperative uterine irritability, miscarriage rate, and preterm labor.

It is mostly done during the second trimester [12], but can be effectively completed up to 34–35 gestational weeks [96, 97]. For gasless laparoscopic surgery (GLS), see Sect. 3.2.2.2.

### 6.9.1.2 Adnexal Preservation or Resection

Traditionally, AT was treated aggressively with salpingo-oophorectomy of the involved side; unwinding the torsion was condemned for fear of releasing a potentially fatal embolus [98, 99]. This was not confirmed [22, 100], and current conservative operative management involves unwinding the adnexa and assessing its viability. Once torsion is unwound, the adnexa show one of the following:

- no evidence of ischemia or mild ischemia with immediate and complete recovery (Fig. 6.7),

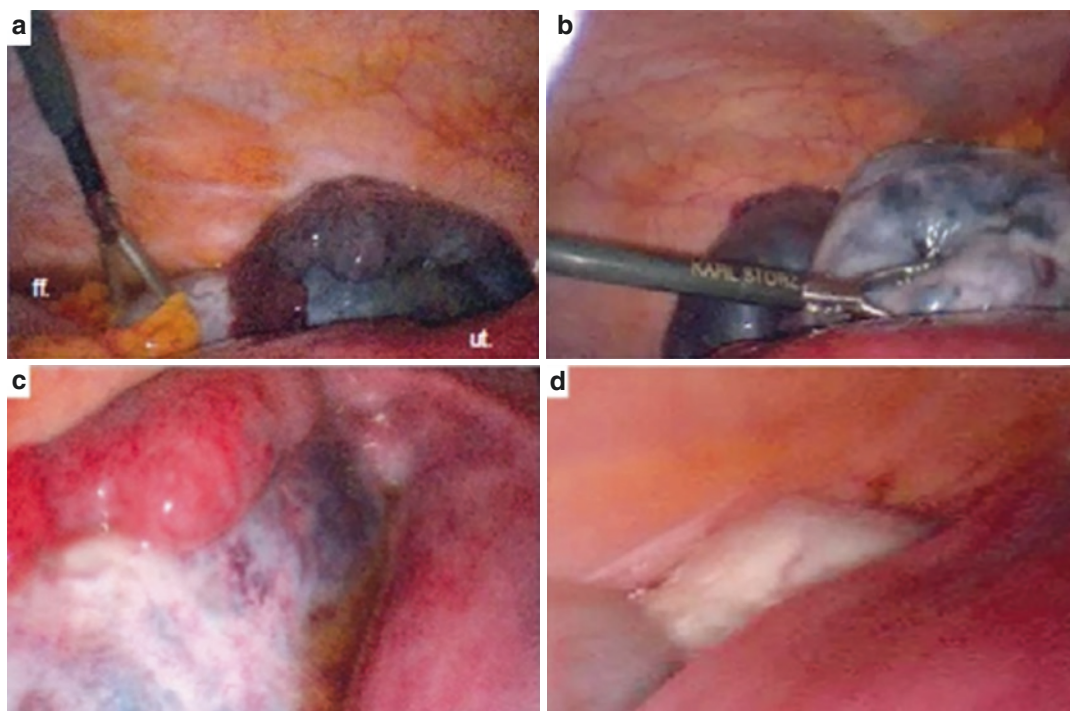
- severe ischemia with a dark red or black tube and ovary, and partial recovery after the pedicle is untwisted (Fig. 6.8),
- gangrenous adnexa without recovery (>48 h).

Only the gangrenous adnexa needs complete removal of the adnexa; the first two situations can be conservatively treated with detorsion and preservation of the ovary, even after severe ischemia has occurred [22]. In <10 min, vascular recovery of the ischemic ovary is completed [54, 71].

(Para)ovarian cyst requires complete cystectomy for a histological diagnosis [100] and prevention of recurrence. Untwisting the pedicle of the cyst should be avoided to prevent emboli and toxic substances related to hypoxia from entering peripheral circulation.

Routine ovariopexy after detorsion does not seem warranted because the risk of retorsion is very low when a cause is found and treated [100]. Despite the necrotic, hemorrhagic, or bluish-black appearance of a torsed ovary, detorsion saves over 90% of these ovaries, and ovarian function recovers [20, 22, 23, 82, 101]. Even with complete ischemia, gross appearance does not correlate with the outcome, and detorsion within 24 h did not show an increase in free radical reperfusion injury [102]. The delay of intervention for 36 h results in significant congestion and necrosis [102]. Assessment of ovarian viability, such as US visualization of follicular development, inspection during a subsequent procedure, observed response to stimulation during IVF, and documentation of fertilization of oocytes from the ovary, has consistently shown that the ovary does recoup function after torsion and detorsion [20, 22, 23, 26, 101]. Furthermore, conservative management with detorsion is encouraged because an increased risk of thromboembolism has not been associated with detorsion procedures [20, 23]. In the general female population, overall morbidity with salpingo-oophorectomy (12%) was significantly higher than in the con-





**Fig. 6.8** (a) Torsioned right ovary; (b) detorsion of the ovary; (c) 3 min after detorsion; (d) normal left ovary. *ut* uterus, *ff* free fluid. (Reproduced with permission from [54] under the CC BY 3.0)

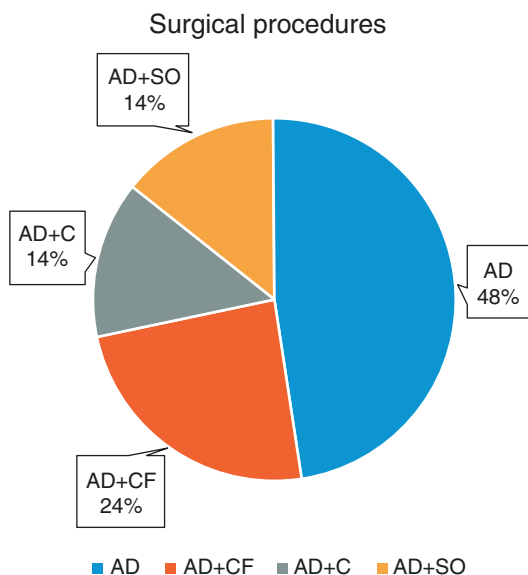
servatively treated group (3%) [103]. Adnexectomy can be avoided, and fertility preserved [59]. After unwinding, aspiration of ovarian cysts, if present, is recommended [85].

Since the successful laparoscopic nonresectional management of AT in the general female population by Mage et al. in 1989 [100] and Bider et al. in the pregnant population in 1991 [49], its use has been more common in pregnancy. Approximately 60% are treated with laparoscopy during pregnancy, mostly in the first trimester (75%) [68], with cases in the early third trimester [85]. The patients who underwent laparoscopy had a significantly smaller ovarian mass. After laparoscopic detorsion, 24 h of postoperative observation is recommended [104, 105]. The operative procedures include detorsion followed by cystectomy in 80%, oophorectomy in 10% for masses >12 cm, and simple detorsion in 10% [68]. Detorsion is successful between 50% and 100% [14, 48, 49]. The distribution of different procedures is presented in Fig. 6.9.

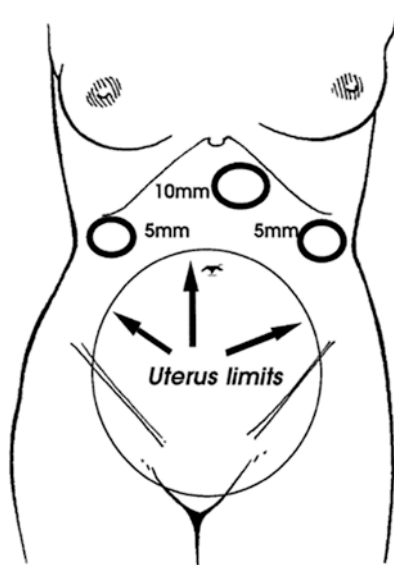
### 6.9.1.3 Underlying or Concomitant Disease

Particular attention should be placed on AT in patients with OHSS. First, the diagnosis is delayed due to other symptoms and signs of OHSS that can mask AT, making AT's prognosis worse. Second, moderate or severe OHSS can present with symptoms and signs of increased intra-abdominal pressure or even abdominal compartment syndrome (see Chap. 22).

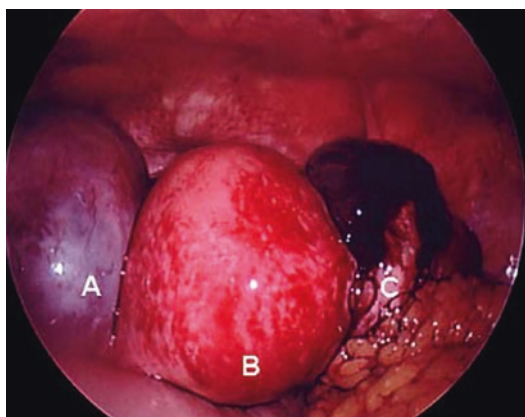
There are cases of AT with concomitant other emergent abdominal conditions, such as contralateral tubal ectopic pregnancy (Fig. 6.10) [106, 107] or acute appendicitis [63]. In contralateral tubal ectopic pregnancy cases, it is important to make an early diagnosis and laparoscopic exploration to save the detorsed adnexa because salpingectomy or adnexectomy is commonly indicated in the contralateral adnexa due to ectopic pregnancy. Such procedure preserves fertility.



**Fig. 6.9** Type of the surgical procedures in adnexal torsion during pregnancy. AD adnexal detorsion, CF cyst fenestration, C cystectomy, SO salpingo-oophorectomy. (Reproduced with permission from [12] under the CC BY Attribution License)



**Fig. 6.11** Trocar position depends on the upper limit of the uterus. Trocars for laparoscopic detorsion of adnexal torsion are inserted in the same vertical body lines and positioned 2–4 cm cranial of the upper limit of the uterus. (Modified and reproduced with permission from [85])



**Fig. 6.10** Adnexal torsion (A) and concomitant contralateral ectopic pregnancy (C). B uterus. (Reproduced with permission from [107])

## 6.9.2 Operative Techniques

### 6.9.2.1 Detorsion/Unwinding

#### Laparoscopy

A small incision of 2 cm is made in the left upper abdominal quadrant (Fig. 6.11), and a 10 mm tro-

car is introduced as an open (Hasson) technique on the left side of the epigastrium. Pneumoperitoneum is induced with an insufflation volume of CO<sub>2</sub> of 1 L/min and an intra-abdominal pressure of 10 mm Hg. The patient is kept in a horizontal position. Secondary trocars are inserted at opposite sites, one in the right upper abdominal quadrant and the other on the extreme left of the middle abdominal quadrant. These secondary trocars are inserted under direct laparoscopic control. Two atraumatic probes are introduced into these trocars: one on the left side, allowing washing and gentle pressure on the uterus in a brief lateral Trendelenburg position, and the other probe elevating the twisted adnexa, pushing it contralaterally to the direction of rotation. The aid of two probes without grasping the tissue avoids bleeding. Serial manipulations achieve the unwinding of the adnexa. The release of pressure ensures the normal positioning of the adnexa. The lateral Trendelenburg position is then abandoned, and after abundant washing, the procedure is stopped for 10 min, with disinflation of the abdominal cavity. Once the procedure is

resumed, the pedicle of the ovary and the tube are examined. An improvement in color and a decrease in edema should be noted. These signs establish the beginning of the recovery of the adnexa, which should turn pink shortly after the procedure. Aspiration of ovarian cysts, if present, is recommended. However, this is not always possible since cysts are often filled with clotted blood.

Cardiotocography should be carried out during the entire procedure [85].

### Single Incision Laparoscopic Surgery

Recently, AT was treated by single incision laparoscopic surgery (SILS, LESS, SSA) [108, 109].

An advantage of SILS is laparoscopy with open abdominal wall access, minimizing the possibility of intra-abdominal injury. It is suitable until 20 weeks gestation, when the uterus is below the umbilicus (Fig. 6.12a). A single port is introduced through a 2–3 cm vertical umbilical incision to the peritoneal cavity (Fig. 6.12b). Layer by layer, the peritoneal cavity is entered; then, 0 polyglactin 910 sutures are placed at each side of the fascia (as stay sutures to help in final closure at the end of the procedure). The SILS device is inserted into the transumbilical incision. The cyst or adnexa are resected intra- or extracorporeally (Fig. 6.12c) [108].



**Fig. 6.12** (a) The site of the twisted ovarian mass at the right upper quadrant (*circle*) and the pregnant uterus location (*dotted line*); (b) the transumbilical SILS device

insertion; (c) extracorporeal ovarian cystectomy; (d) closing the skin incision. (Reproduced with permission from [108] under the CC BY 3.0)

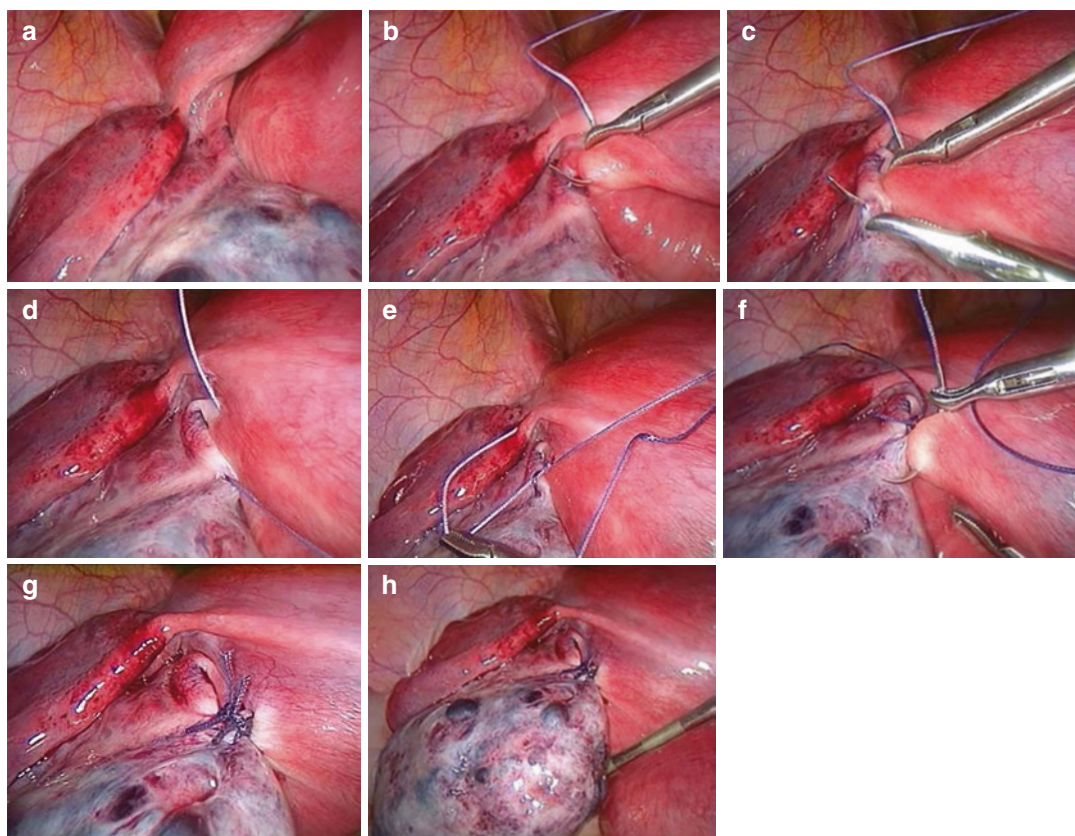


The SILS advantages include better cosmesis (Fig. 6.12d) because of a hidden umbilical scar and the need for fewer trocar incisions, a possible decrease in morbidity related to the visceral and vascular injuries during trocar placement, reduced risk of postoperative wound infections and hernia formation, and elimination of multiple trocar site closures. Another potential merit of SILS is reducing postoperative pain and narcotic use.

### 6.9.2.2 Ovariopexy (Oophoropexy)

In cases where flows return to normal, performing oophoropexy to eliminate retorsion is controversial. Although some studies advocate oophoropexy to prevent a recurrence, a consensus has not been reached.

Germain et al. in 1996, described oophoropexy in the general female population to prevent recurrence by “triplication” of the utero-ovarian ligament [110]. The ligament is plicated and shortened with a running stitch; ovariopexy, where the ovary is sutured to the posterior aspect of the uterus or the lateral pelvic wall; and oophoropexy, where the utero-ovarian ligament is sutured either to the posterior aspect of the uterus or to the lateral pelvic wall (Fig. 6.13). Oophoropexy, although not evaluated in randomized trials, has been done in women of all ages and during pregnancy. Although not commonly done, laparoscopic oophoropexy has good results and is recommended for childhood torsion and in women after an oophorectomy for prior OT [39,



**Fig. 6.13** Oophoropexy of the recurrent torsion of the left ovary at 15 weeks' gestation. (a) Intraoperative finding after ovarian detorsion; (b–e) shortening of the proper ovarian ligament by suturing the distal and proximal end

of the ligament for prevention of recurrent ovarian torsion in pregnancy; (f–h) ovarian fixation for the remaining proper ovarian ligament. (Reproduced with permission from [113])

110–113]. Although oophoropexy has been performed successfully in pregnant women, it was felt that the increased vascularity of the area precluded performing this procedure. The ligament is shortened to reduce recurrence from a lengthy utero-ovarian ligament. A grasping forceps is passed through an Endoloop and then used to tent up the utero-ovarian ligament in the midsection. The pretied endoscopic knot is tightened, pulling the ovary close to the uterus and shortening the utero-ovarian ligament [34].

In a review from 2004, 78 cases of AT during pregnancy were reported. The operative access was laparoscopy in 74% and laparotomy in 18%. Sixty-two percent were treated by preserving the ovary. This included unwinding the adnexa with or without cystectomy. In 38%, an oophorectomy or adnexectomy was performed. An oophoropexy was done in two cases [113].

### 6.9.2.3 Laparotomy

A Pfannenstiel incision is used with a known preoperative diagnosis [76]. A low midline incision is recommended with an uncertain diagnosis or significant bleeding. When McBurney's gridiron incision is made for suspected acute appendicitis, it suffices for the operations on the right adnexa [45].

A simple cystectomy is done for an ovarian cyst when malignancy is excluded. When possible, the entire ovary is delivered from the abdominal cavity and surrounded by moist laparotomy pads to avoid intra-abdominal spillage of cyst contents if a rupture occurs. The thin ovarian capsule is carefully incised, usually with a scalpel. Blunt dissection is used to separate the cyst from the ovarian tissue. Electrosurgery can be used on the internal ovarian surfaces for hemostasis, but should not be used near the cyst wall to minimize the risk of cyst rupture [114].

Rupture is inevitable in some ovarian cysts, particularly endometriomas and functional cysts, such as luteomas. If a dermoid is accidentally ruptured, every effort should be made to avoid spilling the irritating sebaceous contents into the peritoneal cavity. If this occurs, prolonged peritoneal irrigation with warmed saline will prevent peritonitis. Likewise, prolonged irrigation with

warmed saline is judicious if the “chocolate” contents of an endometrioma or the fluid content of a potentially malignant cyst spill within the peritoneal cavity. It remains to be determined if these precautions avoid the detrimental effect of intraoperative rupture on stage I ovarian cancer [115].

Regardless of rupture, all cysts should be completely opened after removal, and the internal surface of the cyst wall should be examined for excrescences. When present, a microscopic examination of frozen sections can help determine if intraoperative staging is required. The definitive diagnosis must await careful examination of permanent sections in all cases.

The ovary does not require precise reconstruction as was thought in the past. Reapproximation with internal sutures may help subsequent reformation of the normal ovarian profile. However, sutures on the external ovarian surface should be avoided to minimize the subsequent risk of adhesion formation [116].

## 6.9.3 Obstetric Management

### 6.9.3.1 Prevention and Treatment of Preterm Labor

See Chap. 4.

### 6.9.3.2 Hormonal Pregnancy Support

Ovariectomy during the first trimester necessitates 17 alpha-hydroxyprogesterone caproate 250 mg IM weekly for 4 weeks as progestogen support for the pregnancy [76]. After this period, progesterone is produced by the placenta. Nevertheless, the persistence of pregnancy is possible even after an early lutectomy [13, 117].

Relaxin mediates the lengthening of the pubic ligament, cervical softening, vaginal relaxation, and inhibiting myometrial contractions. Relaxin in the plasma of pregnant women is believed to originate exclusively from the corpus luteum. Plasma levels peak at approximately 1 ng/mL between 8 and 12 weeks' gestation. After that, they decline to lower levels that persist until the term. Relaxin inhibits contractions of nonpreg-

nant myometrial strips, but not those of uterine tissue taken from pregnant women. It also affects cervical remodeling through cell proliferation and modulation of extracellular matrix components such as collagen and hyaluronan [118, 119]. There are no studies about the influence of relaxin after ovariectomy during pregnancy.

### 6.9.3.3 Ovarian Function

Follow-up Doppler US after detorsion shows the ovary's flow and developing follicles that indicate a normal functioning ovary [71]. This is important for subsequent pregnancies [76]. The first follow-up Doppler US should be made on the first postoperative day. The patient can be discharged if the flow is restored and normal.

## 6.10 Prognosis

A reduced fertilization rate had been attributed to reduced flow in the ovarian artery after ovarian detorsion.

### 6.10.1 Maternal Outcome

#### 6.10.1.1 Preservation of Fertilization

The time between hospital admission and surgery is 6–15.5 h and may be significantly shorter in the first trimester. However, several days may pass between the start of symptoms and surgery [26, 48, 59]. In the laparoscopic era, acute symptoms or persistence of complaints means early surgery (<24 h), and treatment is still in time to preserve fertility [59]. Patients in the second and third trimesters are operated on significantly later than in the first trimester. This difference may be due to difficulty assessing the ovaries on palpation and during US examination or because patients with suspected OT are more readily operated on in early pregnancy when the risk from the (laparoscopic) surgery is minimal [48]. In one large study, 50% had surgery within 24 h and 85% within 72 h [68].

A reduced fertilization rate of 40% for oocytes aspirated from a detorsed ovary is significant, compared to 93% from the unaffected ovary. Seventy-five percent of oocytes from the unaffected side and 64% from the affected side developed into blastocysts [120]. In a repeat IVF procedure, retrieved oocytes from laparoscopically detorsed ovaries could be subsequently fertilized. Therefore, detorsion is recommended as the procedure of choice for ischemic ovaries [23].

#### 6.10.1.2 Delivery

After treatment for AT, the subsequent course of pregnancy is generally favorable; spontaneous abortion rates of 8.3–16.6% [12, 14, 26] and preterm birth of 4.8% [12] do not appear to be increased. In one large study, there were 60% of term deliveries, 15% of preterm deliveries (third trimester), 5% missed abortions, and 20% of elective abortions in the first trimester. There is no difference in pregnancy outcomes between laparoscopy and laparotomy [12]. CS for common obstetric indications was indicated in 27%, and 73% underwent vaginal deliveries [68].

#### 6.10.1.3 Risk of Recurrence

Laparoscopic fixation of the adnexa (ovariopexy) or shortening of the utero-ovarian ligament can be done to avoid the recurrence of AT, but this should be the exception rather than the rule [33, 34, 111, 113]. The reported recurrence is 19.5% for pregnant and 9.1% for nonpregnant women; however, 73.2% of pregnant women and 20.8% of nonpregnant women had been treated with ART before torsion [14]. There was no recurrence in a study with five patients during the subsequent course of the pregnancy [59]. Torsion recurrence is higher in patients with OHSS [33, 121].

### 6.10.2 Fetal Outcome

Delivery at the term of healthy babies occurs in 61–83% [14, 48, 49]. In twin pregnancies, fetal survival is near 100% [52]. The mean birth weight is slightly over 3,000 g [122, 123].



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# Isolated Fallopian Tube Torsion

# 7

## Abstract

Isolated Fallopian tube torsion is an extremely rare condition in pregnancy. Less than 50 cases have been published. Risk factors include mechanical, anatomical, physiological, and pathological conditions. The specificity of this condition is that more than 90% develop on the right side, probably due to the protective effect of the sigmoid colon on the left side. Clinical presentation is the same as for adnexal torsion; sometimes, even with abdominal ultrasound, the preoperative distinction between adnexal and Fallopian tube torsion is impossible. Differential diagnosis is comprehensive as for adnexal torsion. The condition appears predominantly on the right, so it is commonly misdiagnosed as acute appendicitis. Therefore, MRI is useful in such presentations. Suspicion of Fallopian tube torsion is an indication for operative intervention. Laparoscopy is the abdominal entry of choice. Detorsion is the procedure of choice even when ischemic changes are present. Without restoration of vitality after detorsion, salpingectomy is indicated.

and a half times twisted and removed by Henry Morris, whom he assisted. The specimen is preserved in the Museum of the Royal College of Surgeons. Hansen reported the first pediatric case in 1922 [2].

The first known description during pregnancy was by J Praeger (Klinikum Chemnitz) in 1899 [3]. He found dark-red cystic swelling, which turned out to be a left Fallopian tube, with a pedicle twisted twice in the direction of the hands of a watch. The ovary was not involved. Contents of the cyst were bloody fluid and detritus. Recovery was complete, and pregnancy was not interrupted. Pozzi's case in pregnancy in 1900 and two cases by Pinard in 1901–1902 followed [4]. Before them, in 1893, Martin described IFTT from ectopic tubal pregnancy [5]. One of the first reviews that included pregnant women was by Hamilton Bell in 1904 [4]. McKerrow, in 1934 [6] and later Savage (Department of Obstetrics, School of Medicine, University of Maryland Baltimore, Maryland, USA) in 1936 [7], collected 13 published cases (some included torsion of both ovary and tube) and added his own.

## 7.1 Historical Perspective

Sir John Bland-Sutton, in 1890, described the first isolated Fallopian tube torsion (IFTT) in adults [1]. It was caused by hydrosalpinx three

## 7.2 Incidence

Torsion of the Fallopian tube (FT) hydatids of Morgagni could cause acute abdominal pain in adolescents, in 25% of adnexal torsions in this subgroup. However, the condition is an uncommon cause of adnexal torsion in adults [8–11].



The incidence of IFTT from previous reports was 1/1,500,000 [8, 12]; however, the incidence appears to be higher. West Hertfordshire NHS Trust claimed 1/125,000 in 3 years. Régad, in 1933, collected 201 cases in the general population with an incidence in pregnancy of 12% [13]. IFTT in pregnancy involves 12–20% of all cases of IFTT [13–15]; others 1/120,000 pregnancies (1991–2000) [14]. The literature since 1900 revealed 60 cases [7, 10, 14–66], including ectopic pregnancy with IFTT. The incidence of IFTT of the normal FT during pregnancy could be increased compared to the general population [6, 7, 67–70]. Others found torsion of hydrosalpinx during gestation [63–66].

The distribution across trimesters is [8]:

|                  |       |
|------------------|-------|
| First trimester  | 13.3% |
| Second trimester | 20%   |
| Third trimester  | 60%   |
| Intrapartum      | 6.7%  |

### 7.3 Etiopathogenesis

#### 7.3.1 Risk Factors

*It is a fact that the Fallopian tube, when distended with simple fluid and blood, pus, or even when gravid, does twist its pedicle.*  
(Sir John Bland-Sutton, 1904)

IFTT in the general female population can occur at any age, mostly under 30. Risk factors are divided into two categories. *Intrinsic factors* include congenital anomalies or acquired FT pathology (hydrosalpinx, hematosalpinx, neoplasm, surgery, autonomic dysfunction, and abnormal peristalsis). *Extrinsic factors* include changes in the neighboring organs such as neoplasm, adhesions, pregnancy, mechanical factors, movement or trauma to the pelvic organs, or pelvic congestion [71]. Broader classification of causes and theories for IFTT in the general and pregnant population includes [8–10, 14, 35, 37, 40, 41, 72]:

- *anatomic abnormalities*: long mesosalpinx, tubal abnormalities, hematosalpinx, hydrosalpinx, varicose veins in mesosalpinx, hydatid of Morgagni, ectopic tubal pregnancy, paratubal cyst,
- *physiological abnormalities*: abnormal peristalsis or hypermotility of the tube (autonomic dysfunction), tubal spasm, and intestinal peristalsis,
- *hemodynamic/hormonal abnormalities*: venous congestion in the mesosalpinx (progesterone effects of edema and increased tissue vascularity),
- *Sellheim theory*: sudden body position changes,
- *trauma, previous abdominal/gynecologic surgery, or disease*: tubal ligation, PID, tubal endometrioma,
- *gravid uterus*: direct mechanical cause and progesterone effects of edema and increased tissue vascularity,
- *external cephalic version* [43],
- *normal Fallopian tube*.

#### 7.3.2 Pathophysiology

The *anatomical theory* hypothesizes that the tubes tend to stretch and elongate with fetal growth during pregnancy. The ovaries come to lie in closer relation to the fundus of the uterus. Since the tube is longer than the covering peritoneum, it assumes convolutions or spirals, and this appearance persists to puberty and sometimes in adulthood. These spirals are considered a predisposing factor and play a part in IFTT.

A *mechanical theory* is that IFTT is a sequential mechanical event in general and pregnant populations. The process begins with the mechanical blockage of the adnexal veins and lymphatic vessels by an ovarian tumor, pregnancy, hydrosalpinx, or pelvic adhesions after tubal infection or pelvic operation. This obstruction causes pelvic congestion and local edema with subsequent enlargement of the FT,



which induces partial or complete torsion [73]. Torsion pronounces venous stasis and subsequent edema. Hypoperfusion determines hypoxic tissue ischemia and whether the degree of twisting is severe enough to exceed arterial blood pressure. The late step represents complete blood stasis and ischemic necrosis. At this stage, cellular damage is usually irreversible, and reperfusion determined by the untwisting is not followed by *restitutio ad integrum*. A twisted FT undergoing necrosis can cause severe infection similar to perforated appendicitis [74]. There can be torsion of the FT accompanied by a paratubal cyst coiling 2.5 times around the ovary, causing ovarian congestion and enlargement [75].

The *trauma* applied to a pelvic organ is tangential and thus has a twisting movement. Symptoms often appear after unaccustomed trauma. The abdominal musculature contractions impact the ovaries; this causes the right ovary to twist to the left and the left ovary to the right.

Excessive FT peristalsis and associated venous engorgement are common with premenstrual tension. Therefore, IFTT is most common in the week preceding menstruation. The veins supplying the adnexal region are longer than the arteries and twist around them when they become congested. Also, overaction of the autonomic nervous system causes abnormal FT peristalsis at this time of the cycle.

Anchoring adhesions, particularly to the fimbriated end of the tube when longitudinal forces cannot be transmitted, result in excessive peristalsis, and the perpendicular or diagonal forces result in FT twisting. Uterine positional changes, e.g., retroversion to anteversion, cause FT positional changes, making it prone to abnormal movements with possible torsion, particularly with anchoring adhesions.

IFTT in pregnancy is more common on the right side with incidence of 90% [8–10, 18, 22, 23, 25, 28, 29, 31, 32, 36–38, 40–44, 72, 75], while only 10% are on the left side [14, 17, 24, 30, 34, 35]. Possible explanations are:

- the left-sided Fallopian tube is less mobile due to its proximity to the sigmoid mesentery [10, 37, 41],
- slow venous flow on the right side, which may result in congestion,
- hypermobility of the cecum and ileum [10],
- cases of right-sided pain are commonly operated on because of the suspicion of acute appendicitis [9, 37], whereas left-sided cases may be missed and resolve spontaneously.

## 7.4 Classification

From published cases, classification of IFTT, depending on whether ectopic pregnancy is present, can be proposed:

- IFTT with normal intrauterine pregnancy,
- IFTT with tubal ectopic pregnancy [16, 50, 76],
- IFTT with ectopic tubal pregnancy and normal intrauterine pregnancy,
- The classification helps in treatment decision-making (see Sect. 7.8.2).

## 7.5 Clinical Presentation

The most common presenting symptom is pain, which begins in the affected unilateral lower abdomen or pelvis (typically at the level of the right uterine angle) and may radiate to the flank or thigh [9, 10, 32, 33, 37, 40, 41, 72]. The onset of pain is sudden and cramp-like. Most commonly, the pain is constant but may be intermittent if partial or total detorsion occurs [22, 33, 37, 41]. Pain duration is usually less than 48 h, but can last up to 10 days [36]. During labor, the pain unrelated to uterine contractions is present [8], or persistent pain is present after (induction of) labor [28]. Other symptoms include nausea,

vomiting, bowel, and bladder complaints, such as urgency but no associated dysuria [9, 10, 14, 17, 22, 37, 40, 41]. Some patients recall previous episodes of similar symptomatology, mostly less intense, indicating recurrent IFTT [42]. Some may have similar episodes after operative detorsion [77]. There is no disturbance of bowel action.

Most commonly, physical examination reveals good general condition and an afebrile state with stable vital signs [17, 22]. Low-grade fever in 15% of patients indicates necrotic changes of the FT [23, 78]. In almost all patients, abdominal tenderness is present, and guarding can develop in advanced cases [8, 40, 41]. Average fundal height corresponds to the period of gestation. The uterus is relaxed with a regular fetal heart without uterine contractions. Tenderness occurs in the lower abdominal quadrant, on the side of IFTT. A tender adnexal mass may be palpable. Pelvic examination may reveal palpable tender, tense adnexal mass associated with cervical tenderness [79]. The vaginal examination shows a closed cervix without any evidence of bleeding or any abnormal discharge. If scant uterine/vaginal bleeding occurs before or with abdominal pain, ectopic pregnancy or IFTT should be suspected [80]. The bowel sounds are normal. Varicose veins in the mesosalpinx can rupture and mimic ectopic pregnancy, or concomitant ectopic pregnancy may be present [16], causing massive bleeding with symptoms and signs of hemorrhagic shock [81].

It is feasible that an IFTT may occur with subsequent spontaneous detorsion. The patient will complain of transient lower abdominal pain, and a definite diagnosis is challenging.

7.6 Differential Diagnosis

With symptoms, signs, and physical findings similar to other common diseases, the diagnosis of IFTT is rarely established preoperatively [8–10, 37, 40, 41, 43, 44, 72]. The correct preoperative diagnosis in pregnancy before 1936 was 0% [7]; until 2009, it was 37% [78]. The preoperative diagnosis of IFTT of normal-sized FT with a nor-

**Table 7.1** Differential diagnosis of isolated Fallopian tube torsion during pregnancy [9, 10, 22, 36, 37, 41]

|                               |
|-------------------------------|
| Acute appendicitis            |
| Intestinal perforation        |
| Colonic diverticulitis        |
| Ectopic/heterotopic pregnancy |
| Pelvic inflammatory disease   |
| Twisted ovarian cyst          |
| Ruptured follicular cyst      |
| Degenerating leiomyoma        |
| Placental abruption           |
| Urinary tract disease         |
| Renal colic                   |

mal appearance of the ovaries is extremely difficult. The differential diagnosis is presented in Table 7.1.

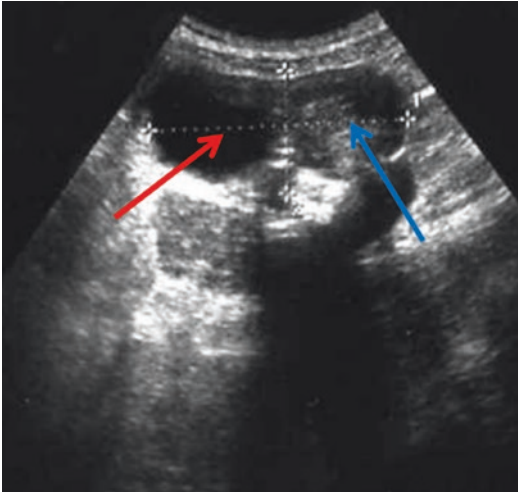
7.7 Diagnosis

7.7.1 Laboratory Findings

White blood cell count and erythrocyte sedimentation rate are mostly normal or slightly elevated [10, 17, 22, 37, 40, 41]. Granulocytosis could be present with a normal white blood cell count [17]. A high white blood cell count indicates IFTT with necrosis [23]. Urinalysis is commonly normal [17, 22].

7.7.2 Abdominal Ultrasound

Transabdominal and transvaginal ultrasound (US) is mandatory [17, 82]. First, the status of the fetus and the placenta should be checked [17], then the pathology searched. The US shows an elongated, convoluted cystic mass with good posterior enhancement (Fig. 7.1), tapering as it nears the uterine corn, with normal ipsilateral ovary [82], free fluid, a dilated tube with thickened echogenic walls, and internal debris or a convoluted echogenic mass [75, 83, 84]. The US findings of IFTT are not pathognomonic and are quite variable [24], especially in the second and third trimesters of pregnancy, where the adnexa are more difficult to visualize. An IFTT is often misdiagnosed as ovarian torsion. The paraovarian



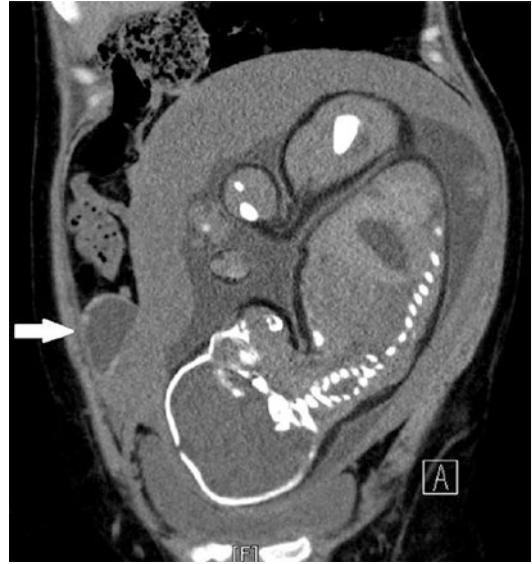
**Fig. 7.1** Two ovoid masses with a thin hypoechoic “bridge” in between. Left-sided mass is anechoic with a small echoic focus posteriorly, while the right-sided mass was hypoechoic with uniform low-level echoes within. They had an appearance of a single bilobed structure with good posterior enhancement. A cyst measuring 3 cm in diameter (*red arrow*) is noted adjacent to the right ovary (*blue arrow*). The right ovary appears slightly enlarged and partly hypoechoic. (Reproduced with permission from [75])

and paratubal cysts are difficult to diagnose when a mass is close to the ipsilateral ovary [85]. However, a clear interface is seen between the ovarian surface and the cyst in most cases, making diagnosis possible. US *Whirlpool sign* of IFTT is diagnostic [86]. Acute adnexal pain with confirmed pelvic cystic structure and normal ipsilateral ovary strongly suggests tubal or paratubal cyst torsion [78]. Varicose veins in the mesosalpinx can rupture and mimic ectopic/heterotopic pregnancy. Transabdominal US rules out hepatobiliary and urologic pathology.

High impedance, reversal, or absence of reverse end-diastolic vascular flow of the tubal wall can be found on spectral Doppler analysis. However, these findings can be difficult to interpret [85].

### 7.7.3 Abdominal CT

CT findings in the general female population (rarely used in pregnancy) with IFTT include an adnexal mass, a twisted appearance to the FT,

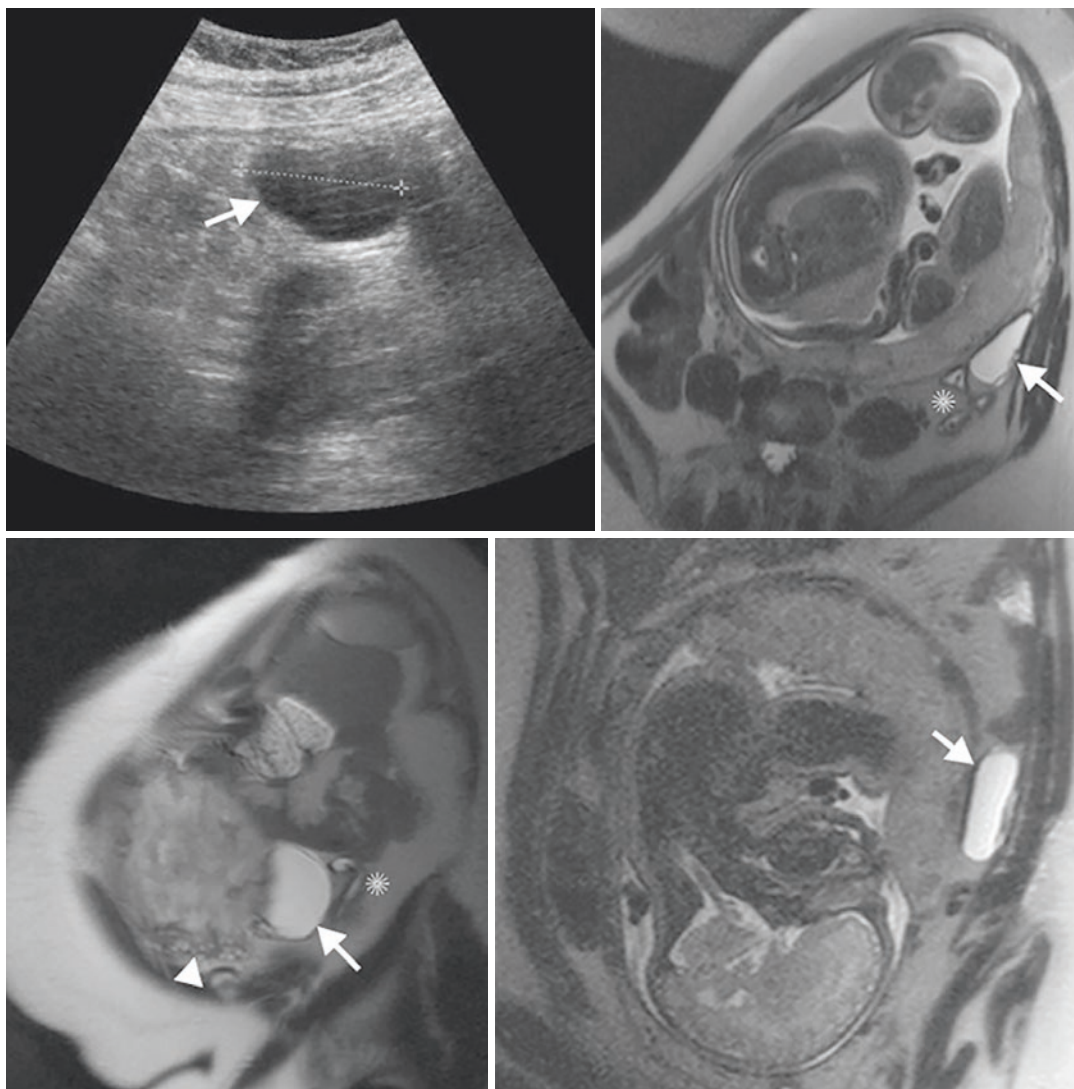


**Fig. 7.2** Abdominopelvic CT shows a 44 × 25 mm-sized homogenous cystic mass (*arrow*) occupying the right lower quadrant. (Reproduced with permission from [46] under the CC BY 4.0)

dilated tube greater than 15 mm, a thickened and enhancing tubal wall, and luminal CT attenuation >50 Hounsfield units consistent with hemorrhage (Fig. 7.2). IFTT or adnexal torsion’s secondary signs include free intrapelvic fluid, peritubular fat stranding, enhancement and thickening of the broad ligament, and regional ileus [83, 87].

### 7.7.4 Abdominal MRI

MRI accurately diagnoses IFTT in pregnancy and is an excellent alternative to diagnostic exploration [29]. By combining an excellent soft-tissue contrast with a large field of view, MRI allows further differentiation of cystic lesions and their relations with intestinal and internal genital structures. T2-weighted MRI findings of dilated and tortuous FT in the presence of a normal ovary (Fig. 7.3) give a clue towards the possibility of IFTT [45]. Excluding bleeding in the dilated FT on T1-weighted images excludes ectopic tubal pregnancy. MRI confirms the *Whirlpool sign* from color Doppler US, helping in an early preoperative diagnosis [45, 86].



**Fig. 7.3** Transabdominal sonography (upper left) and T2-weighted MRI (clockwise starting from upper right: axial, coronal, and sagittal view) of the segmental dilation (white arrow) of the distal left tube. Note the proximity of

the normal-appearing sigmoid colon (*asterisk*) and ipsilateral ovary (*arrowhead*). (Reproduced with permission from [45] under the CC BY 4.0)

## 7.8 Treatment

It is important to distinguish between ovarian torsion and IFTT even if both require a surgical approach. The preoperative knowledge of a normal ovarian structure and vascularization by 2D and Doppler US help preserve a normal-looking ovary or partially damaged due to the adjacent tubal torsion. Thus, it would be possible to pre-

serve ovarian function while avoiding premature loss of the corpus luteum gravidarum in early pregnancy cases and other adverse obstetric sequelae [37, 43]. Second, the preoperative knowledge of a normal ovary reduces patients' preoperative anxiety related to eventual oophorectomy. On the other hand, if the patient does not want any more children, operative sterilization could be performed during the emergent opera-



tion [36]. Third, reducing unnecessary oophorectomies prevents medicolegal issues when the histology shows normal ovarian parenchyma.

## 7.8.1 Abdominal Entry

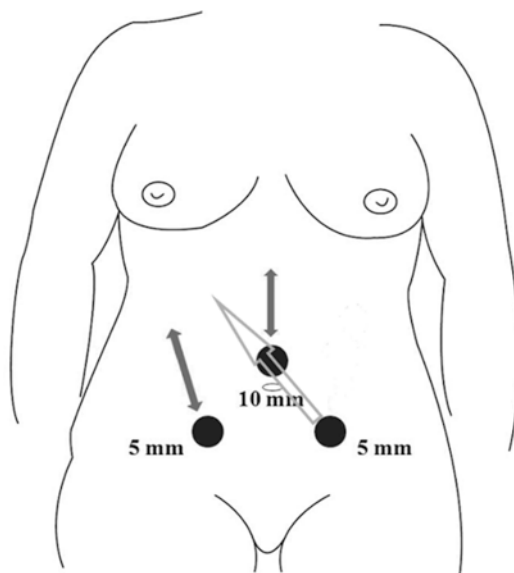
### 7.8.1.1 Laparoscopy

In the general population, laparotomy is common [8, 10, 37, 40, 41, 43, 72], but laparoscopic surgery is steadily increasing [9, 14]. It is recommended as access of choice in the general population [88]. Generally, laparoscopic surgery is safe in all trimesters of pregnancy. Successful cases of IFTT were performed during the first [55], the second [29, 51, 54], and the third trimester [26, 27, 33, 49]. The advantages of the laparoscopic approach are (1) faster recovery, (2) better cosmesis, and (3) fewer pelvic adhesions, which are particularly important for women of reproductive age who wish to preserve fertility.

During the first and second trimesters, trocars are positioned in standard fashion. In the third trimester, depending on the height of the uterus, the Veress needle should be inserted 2–4 cm cranially from the upper border of the uterus, or in *Palmer's point* [27, 54] or open approach with Hasson trocar [29]. The position of other trocars depends on the uterus size and the position of the abnormal findings (Fig. 7.4). Usually, both working trocars are in the right hemiabdomen. The first 5-mm trocar is in the right middle abdominal quadrant, and the second 10 cm above in the midaxillary line [26].

### 7.8.1.2 Laparotomy

Laparoscopy can be used in the third trimester [26, 27, 33], but the patient's large uterus makes the operation more difficult. Therefore, laparotomy is common in the third trimester, primarily when the preoperative diagnosis is unclear. The pararectal incision directly exposes the adnexal field, minimizing or eliminating uterine manipulation, inevitable through an inferior median laparotomy [19]. Another excellent option with preoperative diagnosis is a gridiron incision. It



**Fig. 7.4** Trocar position for laparoscopic access to the twisted Fallopian tube during pregnancy on the right side

results in a short operation, minimal abdominal wall trauma, minimal uterine manipulation, and simultaneous appendectomy [43, 50].

With McBurney (gridiron) incision, it is advisable to make an appendectomy because this incision is reserved for an appendectomy.

After McBurney's incision and appendectomy, there are no diagnostic complexities with right lower quadrant pain in future life. Also, in many IFTT cases, the appendix had gross changes necessitating its removal along with tubal pathology [43, 50]. If the appendix appears inflamed or changed, it should be removed through every incision or laparoscopy [62].

## 7.8.2 Operative Procedures

### 7.8.2.1 Detorsion (Untwisting)

Indications for untwisting (detorsion) are [8, 10, 16, 37, 41, 72]:

- twisting is incomplete or recent,
- ischemic damage appears to be reversible,
- no malignancy or ectopic pregnancy (suspected).

The presence of ischemic changes in twisted FT does not define vitality (Fig. 7.5a). After untwisting, the operator estimates FT vitality (Fig. 7.5b). In some cases, the leading pathology, most commonly the tubal cyst, causes IFTT. Without an indication of salpingectomy, the leading pathology should be resected to eliminate recurrent torsions [19] and provide tissue for histologic analysis. Excision can be performed by bipolar electrocoagulation or with ultrasonic frictional heating instruments. The excision line should be sutured.

Untwisting the pedicle of the cyst should be avoided to prevent emboli and toxic substances related to hypoxia from entering peripheral circulation.

With conservation of the affected adnexa, the inferior surface of the tube is sutured to the round ligament by one or two interrupted atraumatic sutures, and the ovarian ligament is shortened by

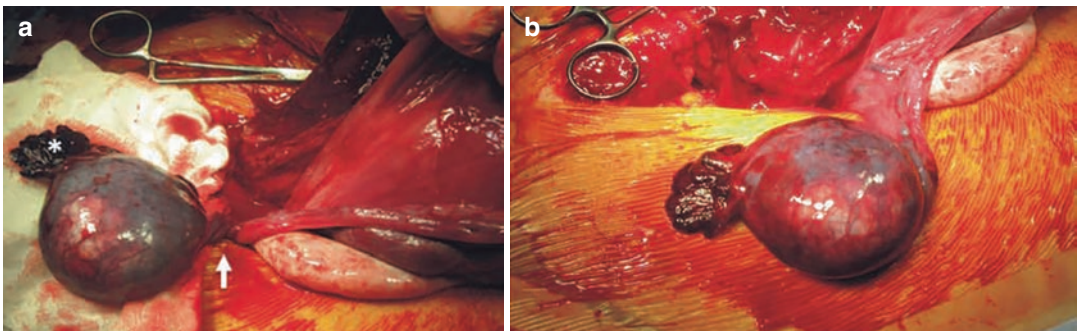
suturing with the uterus. Fixation may change the normal anatomy of the pelvis—either moving the adnexa outside the pelvis or distorting the important close relationship between the ovary and the fimbrial portion of the tube. Branches of the uterine and the ovarian arteries provide circulation to the FT. Shortening a ‘billowing’ mesosalpinx may impair the blood supply to the adjacent ovary.

Tubal detorsion may help preserve fertility, but it may also increase ectopic pregnancy risk, especially in recurrent IFTT [77] due to irreversibly distorted FT with narrowing or obstruction of the lumen due to ischemia or inflammation (see Sect. 7.3.2). The paratubal pathology that leads to IFTT should be excised. A benign cyst could be opened and drained [27].

#### 7.8.2.2 Salpingectomy

There are three indications for total salpingectomy (Fig. 7.6) [17, 23, 32, 36, 42, 76] or partial salpingectomy [22, 80]:

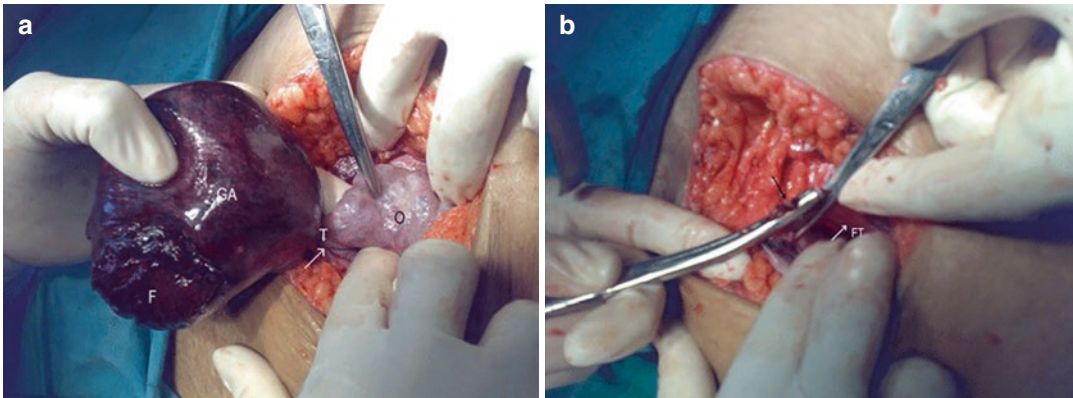
- the tube is beyond recovery (gangrenous, suspected malignancy),
- distended tube causes other organ impairment, such as ureteric compression,
- the tube twisting is associated with ectopic pregnancy.



**Fig. 7.5** (a) An edematous and purple left Fallopian tube showed a three-fold torsion around its long axis (white arrow). The tubal fimbriae were also purple and enlarged

(asterisk). (b) After detorsion of the vital Fallopian tube, prompt revascularization occurred. (Reproduced with permission from [45] under the CC BY 4.0)





**Fig. 7.6** (a) 720° left tubal torsion (*T*). (*O*) Normal-looking ovary, (*GA*) congested and gangrenous-looking tube lateral to the torsion, (*F*) fimbrial end of the tube appearing blocked, leading to hematosalpinx and torsion.

(b) Site of the resection after salpingectomy (*arrow*) and normal-appearing medial end of the tube (*FT*). (Reproduced with permission from [30] under the CC BY 2.5)

The second indication is not absolute. If the ureteric flow is normalized during detorsion, untwisting (resection of leading pathology if present) could be performed. Ovaries should always be preserved unless their perfusions severely deteriorate and necrosis develops. If doubtful, an intraoperative FT biopsy (and ovaries) increases the possibility for tubal preservation if histology shows viable tissue. This is important in women without the contralateral FT for preserving future fertility. After laparoscopic (partial) salpingectomy, the specimen is placed in an endobag to minimize the inoculation of potential endometriotic or malignant tissue [29, 54].

Cesarean section performed first minimizes the hematogenous spread of toxins and eventually bacteria during adnexal manipulation, detorsion, or salpingectomy [46].

### 7.8.3 Obstetric Management

#### 7.8.3.1 Cesarean Section

Indications for Cesarean section (CS) are mostly obstetric. In near-term or term pregnancy, it can be performed with the treatment of IFTT (Fig. 7.7), especially when fetal distress is present [39, 56, 58, 78]. After 32–34 weeks' gestation, a laparotomy could result in (1) the disruption of the abdominal wall wound during (difficult) vaginal delivery and (2) postoperative complications from IFTT surgery on both mother and fetus [22, 46].

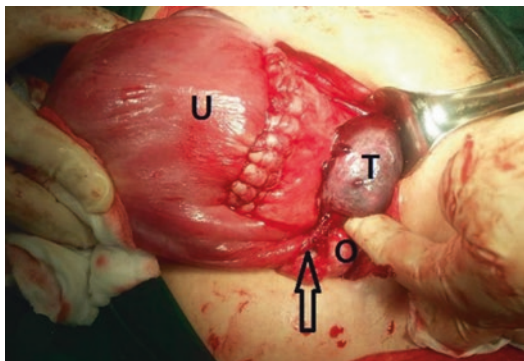
#### 7.8.3.2 Pregnancy Follow-Up

If the pregnancy is undisturbed, all patients should be monitored clinically and by the abdominal US performed 2 and 4 weeks after discharge [17].

## 7.9 Prognosis

### 7.9.1 Maternal Outcome

Even with the necrosis of the FT, maternal outcomes are good. The English language literature concerning twisting or torsion of the FT and pregnancy reported no associated findings during operation in 26.7% of cases. In comparison, associated findings were paratubal cyst in 20%, ovarian cyst in 13.3%, a cyst in the mesosalpinx in 6.7%, a cyst in the broad ligament, sactosalpinx, hydrosalpinx, hematosalpinx, and unruptured tubal ectopic pregnancy. Most cases were treated



**Fig. 7.7** Intraoperative findings of a right ischemic fallopian tubal mass (T) and a grossly normal ovary (O) beside the uterus (U). The isolated torsion of the right Fallopian tube (arrow) was observed at midportion. The suture line of the completed Cesarean section is seen. (Reproduced with permission from [46] under the CC BY 4.0)

with a salpingectomy of the affected FT. In all cases, the pregnancies ended with a favorable outcome (except ectopic tubal pregnancy). Due to the rarity of IFTT in pregnancy, there are no data about the recurrence of IFTT after detorsion. However, recurrence after pregnancy is possible [77].

### 7.9.2 Fetal Outcome

Even with the necrosis of the FT, fetal outcomes are excellent. Even the first known description of IFTT in pregnancy from 1899 resulted in the continuation of pregnancy [3]. There is only one case of miscarriage [53] among 50 published cases.

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## Abstract

Complex ovarian mass is a separate entity from adnexal torsion, which is only one presentation due to ovarian mass and is described in detail in a separate chapter. Complex ovarian mass found in pregnancy is important for several reasons: (1) adnexal torsion, as a result, should be detorsed immediately to preserve ovarian function, (2) persistent pain, (3) ovarian mass rupture and bleeding, and (4) tumor with malignant potential. Persistent pain or compression of surrounding structures is important because it commonly does not subside without surgical intervention. The timing of the operation is critical because intervention during the second trimester carries the lowest risk of obstetric complications. Intra-abdominal bleeding is difficult to diagnose initially, especially if the bleeding is small. Bleeding from the ovarian mass is always the indication for immediate operation. The most difficult issue is asymptomatic and small ovarian mass. Small ovarian mass can commonly be treated conservatively if the malignancy is excluded. There are different imaging and non-imaging methods for confirmation of malignancy. Malignancy status determines the timing and the type of treatment intervention.

*During pregnancy, complex ovarian mass* represents the mass effect and complications of the mass/tumor during pregnancy—adnexal torsion (see Chap. 12), rupture, bleeding, or obstetric complications such as obstruction of labor. Borgfeldt and Andolf defined an adnexal lesion as a simple cyst with the largest diameter of at least 25 mm or a complex cyst of any size.

## 8.1 Incidence and Classification

Adnexal masses detected during pregnancy are the same as those found outside of pregnancy, with the addition of several of them unique to pregnancy (Table 8.1).

The incidence of sonographically (US) detected ovarian masses during pregnancy is 0.05–3.2% [1–5]. A higher incidence of detected adnexal masses is due to the widespread use of the antenatal US and improved imaging technology [6] and possibly a higher mean age of parturients. Outside of pregnancy, the prevalence of an asymptomatic adnexal mass on US is 7.8% in premenopausal women and 2.5% in postmenopausal women [7, 8].

Most cysts are functional (<5 cm) and disappear in 90% by the second trimester of pregnancy [2, 9]. Thus, while 6–17% of adnexal masses resected in the general population are functional



cysts, these are more frequent in pregnancy [10]. The incidence of histopathologically confirmed benign ovarian masses during pregnancy differs (Table 8.2). The most common benign ovarian tumors during pregnancy are cystic teratomas (36–37%), followed by cystadenomas (15–20%) [11–14]. The major concern of an adnexal mass is its potential for malignancy. The incidence of malignancy of these masses during pregnancy is 2–4% [2, 9, 11, 15, 16], and even slightly higher (3.6–6.8%) with persistent masses [3–6, 9, 17, 18], although recent meta-analysis claims 1% [14]. There is a trend of low-stage and low-grade cancers; almost all malignant tumors were grade I and stage IA-IC [2, 11, 19, 20].

There is an equal distribution of benign tumors among part Hawaiian (22.1%), white (18.5%), Filipino (17%), and Japanese (16%). There is an increased incidence of benign cystic teratomas in Filipinas. There is no significant predisposition for nonneoplastic or other neoplastic lesions among the other ethnic groups studied [18].

**Table 8.1** Adnexal masses unique to pregnancy

|                               |
|-------------------------------|
| Hyperstimulated ovaries       |
| Hyperreaction luteinalis      |
| Theca lutein cysts            |
| Luteoma of pregnancy          |
| Ectopic/heterotopic pregnancy |

The risk of adnexal mass rupture in pregnancy is 2% [6]. No articles focused on the risk of rupture concerning size, morphologic appearance, or gestational age.

**8.1.1 Ovarian Cysts**

*Follicular cysts* occur when follicles do not rupture to release an ovum and appear smooth, unilocular cysts with thin walls and clear filled. These typically resolve spontaneously by the mid-second trimester [5, 21]. *Corpus luteum cysts* are less common than follicular cysts, but are more associated with clinical symptoms. A corpus luteum cyst forms after an egg is released from a follicle. It produces progesterone to support a pregnancy until the placenta has formed and lasts until 5–9 weeks of pregnancy. Corpus luteum cysts should resolve around 8–9 weeks of pregnancy, and persistence beyond this should prompt consideration of alternative diagnosis [22]. These resolving cysts are classified as cystic or hemorrhagic corpora lutea based on their appearance on the grey-scale US [3]. Therefore, in the first trimester of pregnancy, ovarian cysts are often functional and generally resolve without complications, and consequently, these were assumed to be physiological [3, 23, 24].

**Table 8.2** Pathology of benign tumors during pregnancy in decreasing incidence

| Type of tumor                       | Torsion | Elective | Cesarean section | Total    |
|-------------------------------------|---------|----------|------------------|----------|
| Teratoma                            | 9 (3)   | 22       | 45 (9)           | 76 (37%) |
| Mucinous cystadenoma                | 1       | 14       | 26 (6)           | 41 (20%) |
| Endometrioma                        | 1       | 8        | 11               | 20 (10%) |
| Corpus luteum cyst                  | 6 (1)   | 4        | 8 (5)            | 18 (9%)  |
| Simple cyst                         | 2       | 6        | 2 (1)            | 10 (5%)  |
| Serous cystadenoma                  | 1       | 1        | 7 (4)            | 9 (5%)   |
| Follicular cyst                     | 1       | 3        | 4                | 8 (4%)   |
| Infarction                          | 7 (3)   | 0        | 0                | 7 (3%)   |
| Paratubal cyst                      | 3 (2)   | 0        | 3                | 6 (2%)   |
| Thecoma/fibroma                     | 0       | 1        | 3 (2)            | 4        |
| Hyperstimulated ovary               | 1       | 0        | 1                | 2        |
| Cystadenofibroma                    | 1       | 0        | 1                | 2        |
| Brenner tumor                       | 0       | 0        | 1                | 1        |
| Multiple luteinized follicular cyst | 0       | 0        | 1 (1)            | 1        |
| Struma ovarii                       | 0       | 1        | 0                | 1        |
| Total                               | 33 (9)  | 60       | 113 (28)         | 206      |

Reproduced with permission from [11]  
Parentheses indicate the number of patients with adnexal tumors undiagnosed before surgery



Eiss, in 1930, reports a case of bilateral tumors, each of which ruptured in pregnancy. Their frequency varies with reports of different series. In Sloane Hospital (1931), the incidence was 1/500 pregnancies; in the University of California Hospital, 1/1500; in McKerron's compilations (1903), it was 1/2500 pregnancies [25]. The number of diagnosed ovarian cysts during pregnancy has increased mainly due to the widespread use of US screening for fetal malformations. Adnexal cysts are found in 4.1–24.9% of pregnant women [26, 27]. Around 92% of ovarian masses are simple, unilocular cysts, and of these, 81.6% are <3 cm in diameter.

The presence of an uncomplicated ovarian cyst is compatible with normal pregnancy, labor, or puerperium [23].

After 16 weeks of gestation, the prevalence of ovarian cysts is 0.5–3.0% [3, 24]. Interestingly, of the ovarian cysts that persisted at 20 weeks gestation, 78.6% were present at the 6-week postnatal scan, and all of these were pathological [3]. Zanetta et al. assessed the prevalence of ovarian cysts at various stages of pregnancy, i.e., in the first, second, and third trimesters [3]. Only 1.2% of the women had an ovarian cyst >3 cm. This figure is significantly lower than the 5.4% published by Condous et al., probably reflecting different population groups. The earlier in gestation US is performed, the more ovarian cysts, particularly functional corpora lutea, will be detected.

As thin-walled vascular structures, such cysts are predisposed to rupture. Bleeding can cause rupture but also can follow the rupture. Also, a torsion can cause the cyst to rupture [28]. Rupture of adnexal torsion during pregnancy may occur secondary to softening of the lesion following stromal decidualization [29]. Bleeding in the corpus luteum is rare and occurs more frequently in younger women [30], primarily when associated with pregnancy [31].

The best predictors of the persistence of adnexal masses during pregnancy are complex masses on US and size >5 cm [6, 32].

### 8.1.2 Ovarian Teratoma

The frequency of ovarian tumors is 1/1000 pregnancies [15] and malignancy in 1/15,000–1/32,000 pregnancies [24]. Mature cystic teratoma (dermoid cyst) is the most common benign ovarian neoplasm discovered during pregnancy (24–40%) [13, 33, 34]. The word teratoma is derived from the Greek word *teraton*, meaning monster, and was used initially by Virchow in the first edition of his book on tumors, published in 1863 [33]. Since mature cystic teratomas are composed of all three germ cell layers, the term “dermoid” is a misnomer. Most of these tumors occur during the reproductive years providing further support for the germ cell theory [33]. It occurs at all stages of life, with most cases between 20 and 30 years of age [13]. In pregnancy, complications increase significantly, including rupture, torsion, infection, and malignant degeneration. As BCT tends to remain in the confines of the true pelvis, it could lead to dystocia and obstructed labor [13].

### 8.1.3 Ovarian Carcinoma

The age shift of childbearing women could cause a change in the histological distribution pattern. Jubb reported 34 cases of primary ovarian carcinoma associated with a pregnancy between 1882 and 1963 [35]; only 54% were of epithelial type [36]. Additional 22 cases between 1963 and 1988 revealed 27% of the epithelial type [37, 38]. In contrast to those previous reports, Dobashi et al. showed that the most common histological types were 80% epithelial, 60% invasive, and 20% *borderline ovarian tumors* (BOT). Of note were the two clear cell carcinomas (20%), which is a relatively high incidence compared to other studies outside Japan; the incidence of ovarian clear cell carcinoma in Japan is the most frequent in the

**Table 8.3** FIGO stage of histologic subtypes of pregnant patients with borderline ovarian tumors [42]

| FIGO stage | Serous | Mucinous | Seromucinous |
|------------|--------|----------|--------------|
| IA         | 19     | 4        | 20           |
| IB         | 1      | 1        | 0            |
| IC         | 5      | 0        | 1            |
| II         | 3      | 0        | 1            |
| III        | 3      | 1        | 0            |

world [39]. The characteristic age group was 30–35, with a high incidence of nulliparity [35]. The age range in Creasman et al. was 18–34, and around 50% were primigravidas [40]. Among pregnancies complicated by ovarian tumors, approximately 8% involve BOT [41] mostly within stage I (Table 8.3). The overall incidence of ovarian cancer in pregnancy is 1/12,500–25,000 pregnancies [43].

**8.1.4 Ovarian Endometrioma**

Decidualization is the process of endometrial change caused by high progesterone levels, which increase glandular epithelial secretion, accumulation of glycogen, and stromal vascularity. These changes create conditions that facilitate the implantation and development of early gestation. The formation of ectopic decidua (deciduosis) during pregnancy is caused by progesterone’s effect on the ectopic endometrium, resulting in endometriosis [44].

Ovarian endometriomas account for 4–5% of ovarian cysts diagnosed in early pregnancy [3] and 11.5% of all adnexal masses during pregnancy [5]. Endometriomas have features common with neoplasia, such as clonal proliferation, consistent with the endometriosis disease theory, and associated with subtypes of ovarian malignancy, such as endometrioid and clear cell carcinoma [29].

**8.2 Clinical Presentation**

Presentations include (1) (a)symptomatic mass, (2) mass or adnexal torsion (see Chap. 6), (3) mass rupture, (4) mass bleeding, (5) malignancy,

or (6) labor obstruction. Adnexal torsions, mass ruptures, or mass bleeding are acute abdominal conditions.

Simple or functional cysts commonly do not cause symptoms and other smaller adnexal masses. Most of these adnexal masses are diagnosed incidentally during the first-trimester screening US [45]. Symptoms were noted in 56.2% during pregnancy and 6.8% during the puerperium [46]. The large tumor may cause pressure symptoms (mass effect), varying from discomfort, dyspnea [47], bladder irritability, etc., to actual pain. Both symptoms and cyst complications during pregnancy and the puerperium were far more frequent with abdominal than with pelvic ovarian tumors and more frequent with cysts of other sorts than dermoids. Cyst complications occur in 20% of patients [46]. Torsion is an essential concern of pregnancy-associated adnexal masses, with a higher incidence (13.8%) than malignancy (3.4%) [11].

Corpus luteum cysts more frequently attain a larger size than follicular cysts. Corpus luteum cysts often delay the onset of the menstrual period, and when it occurs, they may be heavy (*Halban’s syndrome*). Because the cysts are usually larger than follicular cysts and associated with intraluminal bleeding, pain may be a common complaint. The cysts usually regress spontaneously and resolve in 4–8 weeks. Corpus luteum cysts are very vascular, and severe life-threatening bleeding may occur with rupture. On the contrary, rupture of a follicular cyst may cause an acute onset of pain that is usually short-lived. A delayed menstrual period, acute pain, pelvic mass, and hemoperitoneum suggest a ruptured corpus luteum cyst.

Common symptoms of malignant ovarian tumors during pregnancy are excessive generalized enlargement of the abdomen and lower abdominal pain. Approximately 21% present with an acute abdomen from carcinoma complications such as rupture, torsion, or strangulation [35]. Around 66% of ovarian carcinomas are asymptomatic [48]. McKerron collected 1290 cases in 1903, with 80% of small tumors occupying the pelvis during pelvic examinations in labor [25]. The absence of symptoms in 25% shows the

necessity of routine antepartum examinations [46]. The physical findings are often misleading. Hard semisolid dermoids or cystic tumors made tense by pressure may be mistaken for fibroids or vice versa. The abdominal distention with large flaccid cysts and fat abdomen may be confusing. Ascites is common with cysts but rarely occur with fibroids. Pelvic examination usually reveals diffuse pelvic tenderness, often lateralized to the side of the cyst, with a palpable mass. A palpable mass on pelvic examination should be characterized by contour, firmness, size, location, and mobility. The rectovaginal examination with palpation of the uterosacral ligaments and cul-de-sac assesses metastatic disease, nodularity, or obliteration of the cul-de-sac.

Severe bleeding results in abdominal distention and shock.

### 8.3 Differential Diagnosis

The acute pain associated with a blood-filled corpus luteum cyst rupture is indistinguishable from a ruptured ectopic pregnancy. A  $\beta$ HCG level may help distinguish these two entities. Differential diagnosis is presented in Table 6.2.

## 8.4 Diagnosis

### 8.4.1 Laboratory Findings

WBC and CRP help to diagnose the infection and its severity. Hemoglobin and hematocrit help in the diagnosis of intra-abdominal bleeding and its severity. In early pregnancy or when the patient is still unaware of the pregnancy, diagnosis of the hemorrhagic ovarian cyst and ruptured ectopic pregnancy can be difficult. The distinction between these entities largely depends on the serum beta-human chorionic gonadotropin ( $\beta$ HCG) level. Elevated serum  $\beta$ HCG levels with no intrauterine pregnancy suggest the adnexal ring heralding an ectopic gestation. In contrast, a negative serum  $\beta$ HCG level makes a hemorrhagic ovarian cyst more likely [49].

For a suspected ovarian tumor, tumor markers should be checked (Table 8.4). The role of

**Table 8.4** Tumor markers in ovarian tumors

| Tumor marker          | Ovarian neoplasm          |
|-----------------------|---------------------------|
| CA-125                | Epithelial ovarian cancer |
| CEA                   | Mucinous ovarian cancer   |
| $\beta$ HCG           | Embryonal carcinoma       |
|                       | Choriocarcinoma           |
| Inhibin A/B           | Granulosa cell tumor      |
| Lactate dehydrogenase | Dysgerminoma              |
| $\alpha$ -fetoprotein | Endodermal sinus tumor    |
|                       | Embryonal carcinoma       |

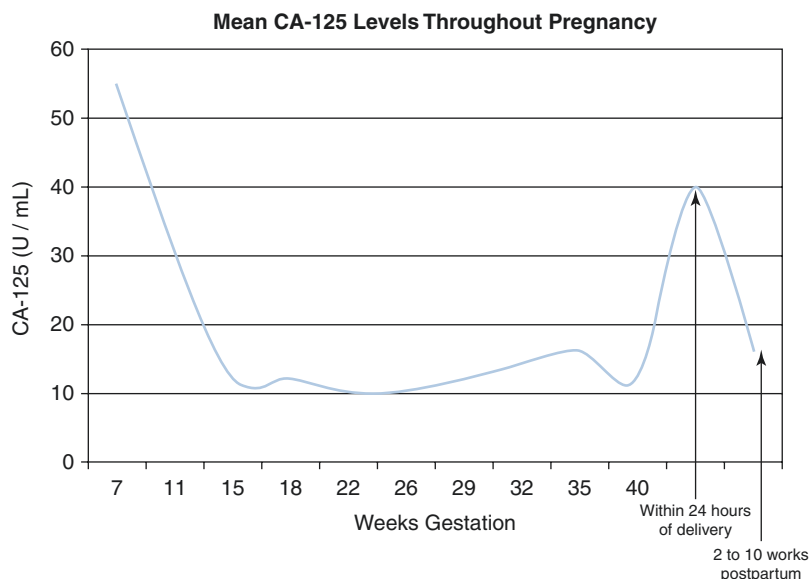
CA cancer antigen, CEA carcinoembryonic antigen, HCG human chorionic gonadotropin

tumor markers is limited in cancer during pregnancy or pregnancy after cancer, mainly due to their low specificity rate. Elevations are not always correlated with malignancy, but are more often associated with normal physiologic changes of pregnancy. Moreover, obstetrical complications can induce even more variations. For example, elevated CA-125 has been related to imminent miscarriage [50], and LDH is known to increase with severe preeclampsia and HELLP syndrome (hemolysis, elevated liver function tests, low platelets) [51]. A high CA-125 has been found in amniotic fluid [52]. It is the oncofetal antigen that is tumor-associated, not tumor-specific. The occurrence of elevated CA-125 levels in PID limits the usefulness of the assay as a cancer test in young women. The normal curve during pregnancy is presented in Fig. 8.1. Measuring CA-125 around the delivery is not recommended [54]. The evaluation of CA-125 is advised for a suspected or indeterminate adnexal mass as a baseline test. It is grossly elevated with malignancy. Its serum level is also valuable for monitoring ovarian cancer treatment responses.

Only CA-125 values can be raised during normal pregnancy, while other tumor marker levels generally remain below the cut-off values [55].

Tumor markers are helpful for both establishing the diagnosis and monitoring the response to treatment.

**Fig. 8.1** Mean CA-125 levels throughout pregnancy [53]



### 8.4.2 Abdominal Ultrasound

*Pelvic ultrasonography remains the first-line examination for the detection and characterization of adnexal masses during pregnancy.*

(Grade C) ([56], French National College of Obstetricians and Gynecologists, 2021)

In a hemodynamically stable patient, transabdominal and transvaginal US is indicated. The mass is easily detected in the pelvis but is often missed if small and behind the uterus, when its presence may not be revealed until after labor. It is essential to define malignancy if the patient is stable, without symptoms and signs of peritonitis or massive bleeding. Three criteria distinguish benign from malignant masses on US: tumor volume, cyst wall structure, and septa structure [45]. Adnexal mass malignancy during pregnancy is commonly described only according to its complex US character, criticized as an oversimplification with a low-positive predictive value for malignancies [57]. Because of morphological similarities, it is unhelpful in distinguishing tumors of low malignant potential from benign neoplasms [9]. *Internal papillary excrescences* can be visualized in 50% of malignancies [41].

There are pitfalls in applying the abovementioned criteria to adnexal masses in pregnancy. First, obtaining good images of adnexal masses after the 20th week of gestation is hard unless the mass is large. Second, technical difficulties exist in evaluating velocimetric features during pregnancy. The vessels and blood flow surrounding the gravid uterus mainly have high velocity and low resistance characteristics with a false-positive rate of nearly 50% [58], but a pulsatility index  $<1.0$  is associated with an increased risk of malignancy [59]. Third, during pregnancy, the major tumor type is of germ cell origin. US characteristics, although not necessarily different from those of epithelial-origin tumors, could be incompatible with the scoring criteria developed for epithelial ovarian cancers. Significantly higher US tumor growth rates are found in ovarian pregnancies. Even growth of 0.35 cm/week has been found [11].

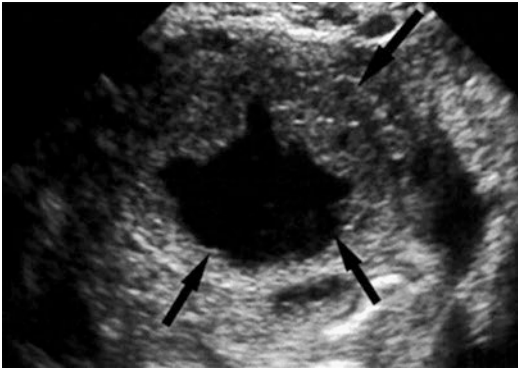
The hemorrhagic ovarian cyst exhibits a myriad of US appearances; most commonly, as a rounded hypoechoic mass containing low-level echoes, fine strands, or septations; however, other patterns are so frequent that the hemorrhagic ovarian cyst has been termed “the great imitator” [60, 61]. Occasionally, a hemorrhagic ovarian cyst presents as a thick echogenic wall surround-

ing a central rounded echolucent area—a pattern remarkably similar to the *adnexal ring sign* (Fig. 8.2) of an ectopic pregnancy. Identifying an intrauterine gestational sac excludes ectopic pregnancy and permits expectant management even with intraperitoneal bleeding [49, 63]. Elevated  $\beta$ HCG can be misleading. In such cases, intrauterine pregnancy (heterotopic pregnancy) should be ruled out.

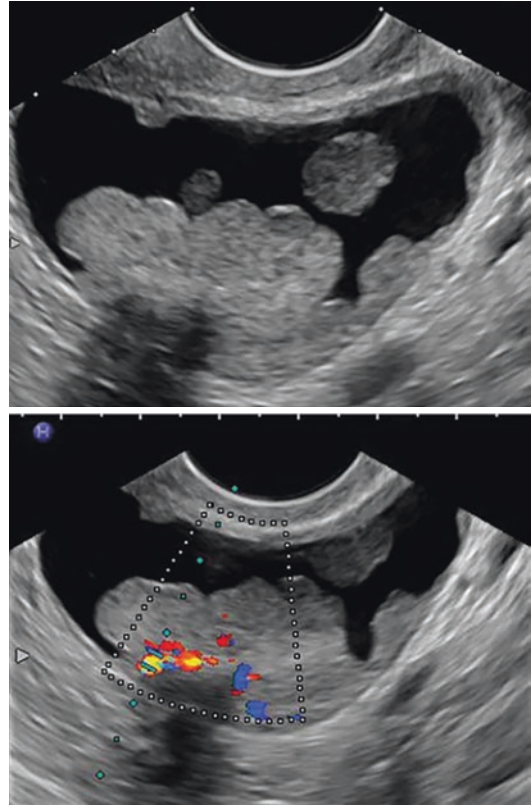
US and color Doppler of decidualized ovarian endometrioma document rapidly growing and abundantly vascularized intracystic excrescences. Conversely, the septations or significant free fluid were never reported (Fig. 8.3). Such masses are difficult to distinguish from BOT (Fig. 8.4a).

For pyosalpinx US characteristics, see Sect. 13.8.2.

In one study, correct US diagnoses included 95% of dermoid cysts, 80% of endometriomas, and 71% of simple cysts. Ten percent of adnexal masses had US characteristics concerning malignancy, but only one was ovarian cancer [5]. The IOTA protocol has recognized US characteristics that accurately predict the risk of ovarian cancer. Another study reviewed 130 cases of adnexal



**Fig. 8.2** Hemorrhagic ovarian cyst simulating a ruptured ectopic pregnancy with severe acute pelvic pain and a positive  $\beta$ HCG. The coronal right adnexal US shows a mass with an irregular thick rind (arrows). This was mistaken for a ruptured ectopic pregnancy, but was identified as a ruptured hemorrhagic cyst at laparoscopy. The patient had a concurrent, early intrauterine pregnancy. (Reproduced with permission from [62])

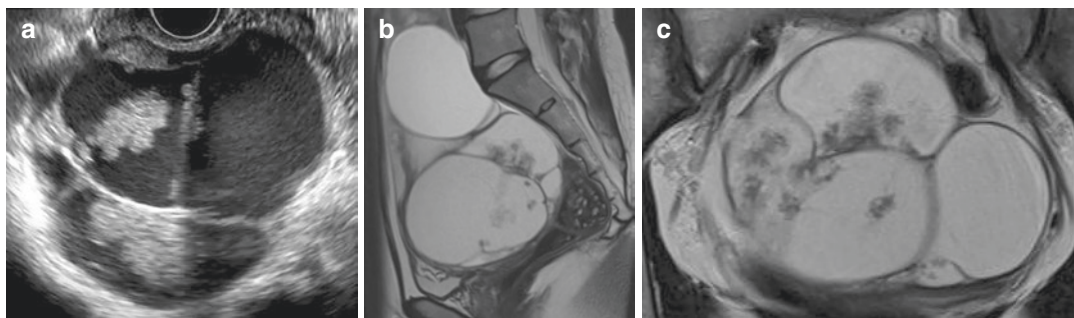


**Fig. 8.3** US of ovarian endometrioma in pregnancy mimicking malignancy. The irregular solid part of the endometrioma protrudes within the lumen of the cyst. Above this excrescence, echogenic debris, mobile under probe manipulation, is noted (*upper panel*). Color Doppler detected multiple vascularization signals index within the solid part (*lower panel*). The resistance index was 0.37. (Reproduced with permission from [64])

masses in pregnancy that required excision or were found incidentally during CS. They found that 89 of 91 resected masses were correctly diagnosed as benign using US [9].

Though some tumors are large, nearly 20% of adnexal tumors are discovered when tumor torsion occurs or incidentally during CS. This underscores the possibility that some patients with vaginal delivery could have failed to have their asymptomatic adnexal mass revealed, thus making the true denominator of these events during pregnancy unknown [11].





**Fig. 8.4** (a) Transvaginal US at 6 weeks of gestation shows a right ovarian multilocular mass 14 cm in diameter with internal papillary pedunculated projections. (b) A plain pelvic MRI (sagittal T2-weighted) reveals a multi-

locular cystic mass with papillary mural nodules. (c) Coronal T2-weighted image shows relatively high, lobulated mural nodules with a pedunculated configuration and hypointense core [42]

### 8.4.3 Abdominal MRI

*Pelvic MRI is recommended from the 12th week of gestation in case of indeterminate adnexal masses and should be concluded with a diagnostic score.*

(ADNEX MR/O-RADS) (Grade C) [56],  
French National College of Obstetricians  
and Gynecologists, 2021)

MRI is better at distinguishing paraovarian cystic lesions, which can be managed conservatively and provide better tissue characterization, allowing for a more accurate evaluation of the large masses that are difficult for visualization on US. MRI can also determine the possible extent of malignancy and aid in diagnosing acute bowel processes such as appendicitis and inflammatory bowel disease [65]. On US, a decidualized endometrioma appears as a loculated cystic mass with vascularized papillary projections, resembling a malignancy [66]. In these cases, MRI helps in the characterization of the mass. MRI is also accurate for defining BOT (Fig. 8.4b, c). The following findings of mural nodules on MRI suggest seromucinous BOT rather than endometriotic cysts with decidual changes: (1) lower signal intensity ratios on T1WI, (2) a higher nodule height, (3) lobulated margins, (4) a pedunculated configuration, and (5) a T2 hypointense core [67]. Gadolinium enhancement is helpful but is contraindicated in pregnancy.

## 8.5 Treatment

### 8.5.1 Introduction

Approximately 51–70% of adnexal masses in pregnancy will resolve spontaneously, and the risk of acute complications is less than 2% [5, 21]. Because of increased complications of ovarian surgery in pregnancy [68, 69], surgical management of ovarian cysts in pregnancy has been reconsidered [17]. Historically, pregnant women with persistent adnexal masses underwent elective removal of the masses in the second trimester [70]; this is no longer an acceptable practice in asymptomatic women, as surgical intervention, in an emergency or after 24 weeks gestation, is associated with a poorer obstetric outcome [16]. Obstetric complications include spontaneous miscarriage or preterm premature rupture of membranes [17].

### 8.5.2 Conservative Treatment

#### 8.5.2.1 Observation

##### Asymptomatic

As only 0.13% of women with an ovarian cyst required acute intervention during pregnancy, the conclusion is that examining the ovaries at the time of a first-trimester scan is of limited value. Expectant management is more common with



regular use of imaging techniques like MRI and transvaginal color Doppler.

Early in pregnancy, ovarian enlargement <6 cm in diameter is usually due to corpus luteum formation. Asymptomatic patients with simple unilocular cysts <6 cm, which do not change, need only periodic US follow-up. Most resolve spontaneously [26, 71]. Corpus luteal cysts regress by 12–16 weeks. For an ovarian cyst in the first trimester, it is better to wait until 14–16 weeks because (1) the implantation of pregnancy is more secure, (2) the cyst may disappear spontaneously, (3) surgical access to the mass is much easier, and (4) progesterone supplementation is mandatory for oophorectomy before this period.

### Abdominal Pain

Those women requiring intervention will present with pain, while prior knowledge of the presence of a cyst may only increase anxiety, even though the risk of complication is very low. If a nonmalignant ovarian cyst is noted at the time of a first-trimester US, a follow-up scan 6 weeks after the pregnancy is recommended. Although there are no randomized clinical trials to determine the optimal management of an adnexal mass in pregnancy, experience suggests that expectant management is safe and without severe adverse outcomes for both mother and fetus [3].

### Borderline Ovarian Tumors/Suspected Malignancy

If a provisional diagnosis of hemorrhagic corpus luteum cyst with minimal hemoperitoneum can be made, expectant management with serial clinical examination and hemoglobin measurements is indicated [30].

A growing understanding of the natural history of BOT allows a more conservative approach (expectant management) as an alternative to surgical management, preserving fertility [72]. After the pregnancy, these patients underwent surgery [3, 73]. No guidelines have been issued regarding

the follow-up of suspicious non-operated BOTs during pregnancy [56]. The issue with BOT is the inaccuracy of preoperative diagnosis. Diagnosis is confirmed histologically in only 33% with US appearance and the presence of papillary projections, nonvascular on color Doppler [72]. The additional surgical dilemma is the size of the tumor. Despite benign characteristics, it can have a high probability of torsion [72]. The review of surgical and histopathological characteristics is presented in Table 8.5.

*For treatment of BOTs during pregnancy, the laparoscopic route should be preferred if feasible (Grade C) [56]. (French National College of Obstetricians and Gynecologists, 2021).*

However, laparoscopy is performed only in the first trimester of pregnancy, while laparotomy is performed throughout pregnancy. Given the rarity of BOTs, there is no definite therapeutic policy for BOTs in pregnancy. Conservative surgery, such as salpingo-oophorectomy or cystectomy, is used in most pregnant patients [42]. As in the general population, the recurrence rate increases for cystectomy (12.5%) compared to salpingo-oophorectomy (3.7%). In addition, recurrence is observed only in serous types and not in mucinous or seromucinous.

*If a serous BOT is suspected in pregnancy, salpingo-oophorectomy rather than cystectomy should be considered [42].*

A similar issue is with *decidualized ovarian endometriomas* during pregnancy. On the one hand, expectant management appears rea-

**Table 8.5** Epidemiological, surgical, and histological characteristics of borderline ovarian tumors detected during pregnancy [42]

|                   |                              |    |         |
|-------------------|------------------------------|----|---------|
| Mean age          | 30.4 years (range 20–42)     |    |         |
| Surgical approach | Laparotomy                   | 37 | (62.7%) |
|                   | Laparoscopy                  | 16 | (27.1%) |
|                   | Laparoscopy + Laparotomy     | 6  | (10.2%) |
| Type of surgery   |                              |    |         |
| Unilateral        | Cystectomy                   | 25 | (48.1%) |
|                   | SO                           | 27 | (51.9%) |
| Bilateral         | Bi-cystectomy                | 1  | (14.3%) |
|                   | BSO                          | 2  | (28.6%) |
|                   | Uni-cystectomy + Uni-SO      | 3  | (42.9%) |
|                   | Bi-biopsy                    | 1  | (14.3%) |
| Histologic type   | Serous                       | 31 | (52.5%) |
|                   | Mucinous                     | 22 | (37.3%) |
|                   | Seromucinous                 | 6  | (10.2%) |
| FIGO stage        | IA                           | 43 | (72.9%) |
|                   | IB                           | 2  | (3.4%)  |
|                   | IC                           | 6  | (10.2%) |
|                   | II                           | 4  | (6.8%)  |
|                   | III                          | 4  | (6.8%)  |
| Restaging surgery | No                           | 33 | (55.9%) |
|                   | Fertility-preserving surgery | 21 | (35.6%) |
|                   | Radical surgery              | 5  | (8.5%)  |
| Restaging         |                              |    |         |
| Upstage           | Yes                          | 6  | (23.1%) |
|                   | No                           | 20 | (76.9%) |
| Recurrence        | Yes                          | 6  | (10.2%) |

sonable, considering that pain symptoms generally improve during pregnancy and that surgery is more demanding and riskier due to the enlarged and pregnant uterus. On the other hand, concerns have been raised regarding the accuracy of US in pregnancy. Of the 27 published cases, 19 (70%) were managed surgically, four were delayed till CS with concomitant cyst excision, and eight were managed conservatively with serial monitoring of the cyst, with spontaneous regression following delivery [74].

#### 8.5.2.2 Ultrasound-Guided Aspiration

Aspiration of simple ovarian cysts during pregnancy is safe and may prevent surgical intervention. In some cases, this is the definitive treatment

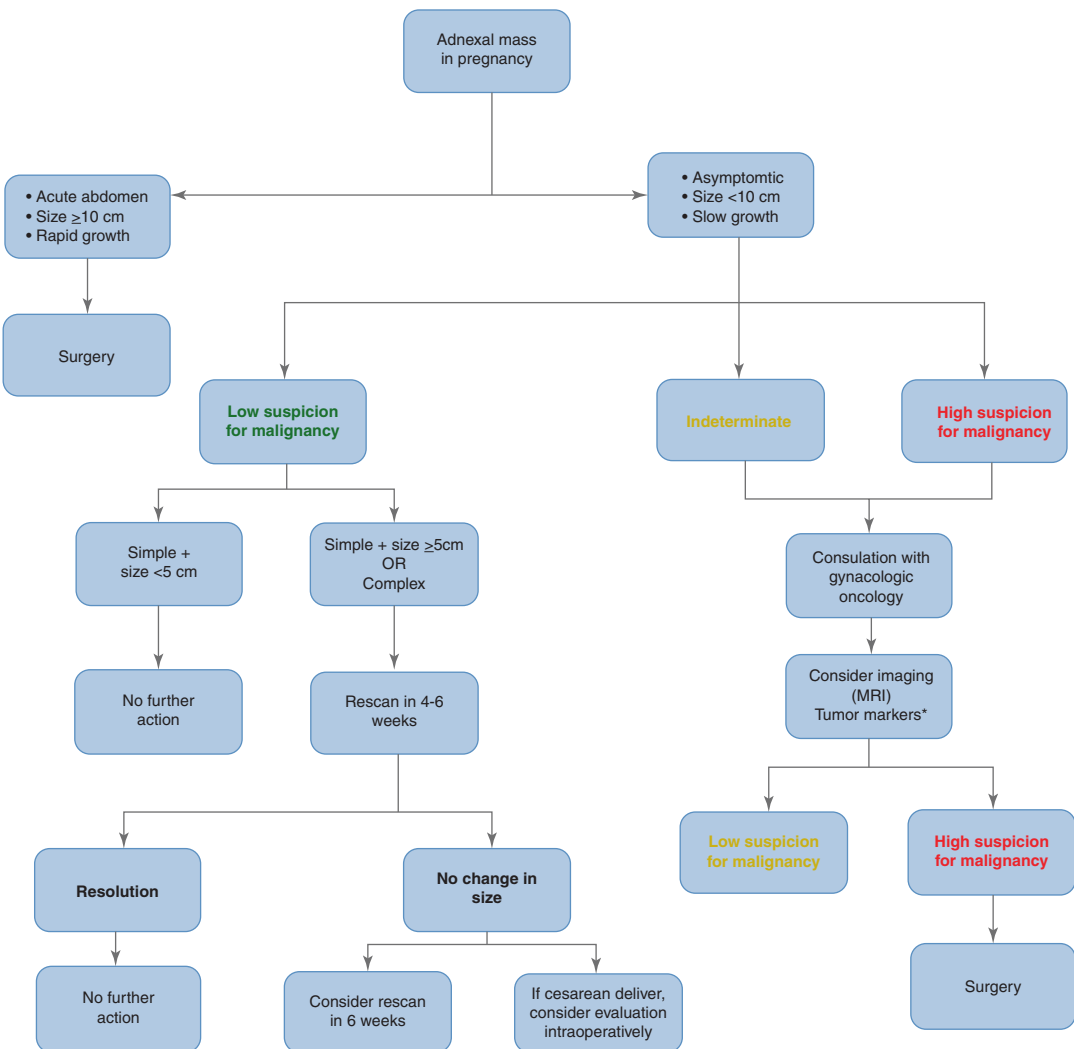
[75]. Neither anesthesia nor analgesia is required for such intervention. The US-guided aspiration to relieve pain generated by simple ovarian cysts in nonpregnant women can be performed either transvaginally or transabdominally, depending on the location of the cyst [76]. After 14 weeks' gestation, the uterus is an abdominal organ, so the ovaries are more easily targeted transabdominally. If the pain persists after the procedure without other symptoms or complications, a laparoscopic ovarian cystectomy after delivery is indicated [3]. Fine-needle aspiration is not appropriate if the cyst has any suspicious morphological features. It is not a common diagnostic problem because the frequency of ovarian cancer in pregnancy is 1/15,000–1/32,000 pregnancies [24].

### 8.5.3 Surgical Treatment

Operative treatment is oriented toward treating complications of ovarian masses during pregnancy. Approximately 1–2.3% of adnexal masses in pregnancy require surgical intervention [77]. Indications for the operation are presented in Table 8.6, while a complete diagnostic-therapeutic algorithm of non-ruptured ovarian cysts in pregnancy is presented in Fig. 8.5. In short, if surgical removal of an adnexal mass is necessary during pregnancy, it should be performed after the first trimester. This recommen-

**Table 8.6** Indications for surgery of adnexal masses in pregnancy

| Emergent operation                        | Early elective operation                                       |
|-------------------------------------------|----------------------------------------------------------------|
| Torsion of the cyst/adnexa                | Mass >6 cm until the second trimester unless uterine leiomyoma |
| Rupture of the cyst                       | Suspected/proven malignancy                                    |
| Infected cyst                             | Fetal malpresentation                                          |
| Urinary retention due to cystic impaction | Intrauterine growth retardation                                |
| Dyspnea due to giant tumor                |                                                                |
| Obstructed labor                          |                                                                |



**Fig. 8.5** Diagnostic-therapeutic algorithm of non-ruptured ovarian mass in pregnancy. Rapid growth—increase in size  $\geq 3.5$  cm/week. (Reproduced with permission from [78])

dation is based on the following: (1) most functional cysts resolve by the second trimester, and a persistent mass has a higher risk of malignancy; (2) surgery during the second trimester has a decreased rate of preterm labor than at later gestations; and (3) surgery during the third trimester is more difficult as the enlarged uterus may interfere with adequate visualization [79].

For adnexal/cyst torsion, see Chap. 6. Intrauterine growth retardation may be either due to the prominent vascularity of the tumor originating from the ovarian vessels or due to the compressive effect of the tumor on the uterine blood supply [80].

### 8.5.3.1 Emergency Laparotomy

A hemodynamically unstable patient or patient with an acute abdomen requires emergent exploration. Emergency laparotomy, not laparoscopy, is immediate and definitive surgery in hemodynamically unstable patients. The second indication for emergency laparotomy is fetal distress when definitive surgery is performed after CS. The third indication is obstructed labor due to ovarian cyst/tumor when CS followed by definitive surgery is recommended.

Rupture and bleeding with hemodynamic stability do not preclude diagnostic and therapeutic laparoscopy.

### Hemorrhagic Corpus Luteum

A hemorrhagic corpus luteum cyst with minimal hemoperitoneum may be served expectantly [30]. However, massive or prolonged hemorrhage requires emergent surgical intervention [31]. In hemodynamically stable patients, laparoscopic treatment is preferable [81, 82]. Further, utilizing intraoperative autologous blood transfusion, transfusion of bank blood can be avoided even with massive hemoperitoneum due to ruptured corpus luteum cyst in patients with ectopic pregnancy [81, 82].

### Ovarian Teratoma

Ruptured BCT of the ovary mimicking gynecological malignancy is uncommon and could be misdiagnosed [83]. Intra-abdominal peritoneal seedlings, adhesions, or masses are a frequent

sequel. In most cases, abdominal seedlings are essential for mature neuroglial elements, and the long-term survival rate is good. Recognizing a dermoid tumor associated with the glial seedling is essential to avoid unnecessary debulking surgery. Conservative management seems to have a good prognosis following postoperative adhesions, fibrous bands, or obstructions.

### Obstructed Labor

As for any other cause, an indication for emergent CS and ovarian mass operation during pregnancy is the risk of obstructed labor by ovarian mass, with an incidence of 17–21% [65].

### 8.5.3.2 Elective Laparotomy

Indications for early elective operations are cysts >10 cm in diameter due to increased risk of malignancy, rupture, or torsion. Management of cysts ranging from 5 to 10 cm is controversial. Surgical intervention is recommended if the cysts contain septae, nodules, papillary excrescences, or solid components.

### Ovarian Teratoma

Treatment of suspected ovarian teratoma is surgical removal as soon as possible after diagnosis to avoid complications. They may be responsible for torsion, rupture, and obstruction during labor. Over 200 cases of BCT in pregnancy have been reported, and many of them ruptured spontaneously or iatrogenically. A review of 47 cases showed minimal spillage in 42.5% during cyst extraction and none developed chemical peritonitis [84]. Rupture is rare but can cause complications such as chemical or granulomatous peritonitis, mimicking advanced ovarian malignancy [13, 83]. The rupture or leakage of cyst fluid should be avoided during the operation. If it happens before or during the procedure, copious saline washing should be performed to minimize chemical peritonitis and its sequel, including further surgeries to treat the complications [85, 86]. Granulomatous peritonitis from ruptured ovarian teratomas results in numerous nodules of mature glial tissue implant on the peritoneal surface. This diffuse peritoneal reaction mimics

advanced ovarian malignancy, and commonly surgical staging is performed [13, 83].

Incidental BCT in the first trimester of pregnancy should be surgically removed at 14–16 weeks of gestation to avoid the risk of damage to the corpus luteum. If the diagnosis of BCT occurs at 16–22 weeks, surgery should be performed as soon as possible. If discovered after 22 weeks of pregnancy, the treatment may be deferred until delivery [13].

### 8.5.3.3 Minimally Invasive Surgery

#### General Considerations

The pathophysiology of laparoscopy is discussed in Sects. 3.2.2.2 and 6.9.1.1. Ovarian tumors or cysts can be easily removed until 28 weeks of gestation; manipulation is difficult in later gestation and may precipitate preterm labor.

Laparoscopic compared to open surgery for removing adnexal masses in pregnancy had the following outcomes: no difference in fetal loss or operative time; decreased or similar blood loss, similar rates of preterm labor and spontaneous abortion, and shorter length of hospital stay [14, 87].

#### Gasless Laparoscopy

See Sect. 3.2.2.2.

#### Robotic or Single-Site Surgery

Robotic resection of adnexal masses during pregnancy is safe and feasible, with similar surgical outcomes as laparoscopy. The robotic cohort had a significantly shorter hospital stay and estimated blood loss [88]. Single-site/Single port surgery for adnexal masses in pregnancy demonstrated the feasibility, safety, and putative benefits. Resected ovarian mass can be extracted through the same abdominal wall incision where the port was introduced, eliminating the need for additional abdominal wall trauma from additional stab incisions [89, 90]. This is particularly important for the masses that cannot be decompressed or aspirated (see Sect. 8.5.3.3). For principles of single port surgery, see Sect. 6.9.2.1 and Sect. 8.5.4.2.

#### Cystectomy

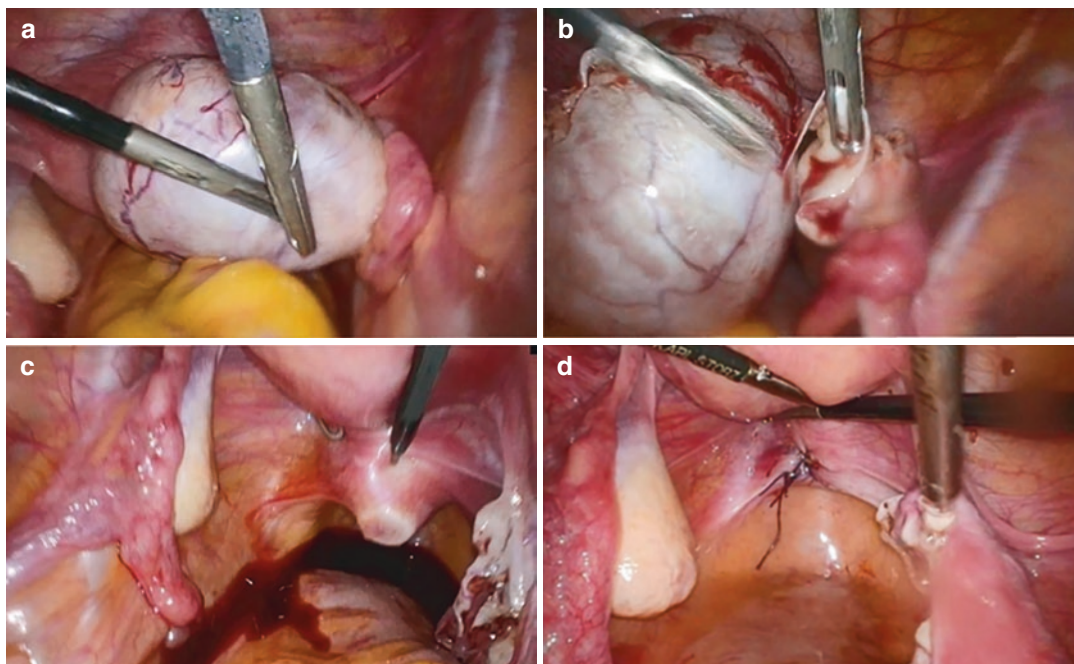
*Laparoscopy is a safe and effective treatment in gravid patients with symptomatic ovarian cystic masses. Observation is acceptable for all other cystic lesions, provided ultrasound is not concerning for malignancy and tumor markers are normal. The initial observation is warranted for more cystic lesions less than 6 cm in size. (SAGES, 2011 [91])*

Nezhat et al., in 1991, first described laparoscopic cystectomy in pregnancy [92]. Conservative surgical therapy removes the cyst and coagulates its base (Fig. 8.6a, b). Large cystic masses may require decompression/aspiration to fit through a small incision. Spillage can be minimal or nonexistent by decompressing a cyst into a laparoscopic bag. Copious irrigation also helps to keep the residual content to a minimum (see Sect. 8.5.3.2). Another option to avoid cyst rupture and spillage during surgery is the transvaginal extraction of the specimen. Minimizing the risk of disruption and fragmentation of the lesion during extraction is accomplished through posterior colpotomy due to the elasticity of the vagina (Fig. 8.6c, d). An additional benefit is avoiding the extension of abdominal wall incision for specimen extraction resulting in reduced postoperative pain and better cosmesis [93].

After cystectomy, the ovarian incision can be left open or approximated by three techniques:

- Fine monofilament suture of the edges,
- Tissue glue,
- Coagulation of the ovarian cortex adjacent to the surface.

Stitching is necessary to avoid adhesions between the raw ovarian surface and the raw peritoneal surface left after bowel adhesiolysis in the left adnexa [94].



**Fig. 8.6** (a) Laparoscopic appearance of the borderline ovarian tumor. (b) Laparoscopic cystectomy without rupture of the capsule or spillage of the content. (c) Delineation of the posterior fornix to perform colpotomy

for the introduction of the endobag and transvaginal extraction of the specimen. (d) Final view of the pelvis at the end of the operation. (Reproduced with permission from [93])

#### 8.5.3.4 Incidental Tumors

If an incidental adnexal mass during CS has characteristics suggestive of malignancy, it should be removed and sent for a frozen section. Adnexal masses >5 cm removed by cystectomy do not have a higher rate of complications or increased morbidity or mortality attributable to cystectomy [95, 96].

Adnexal mass >5 cm should be removed during CS [95].

### 8.5.4 Anesthetic and Perioperative Management

See Chap. 21.

#### 8.5.4.1 First Trimester

After the corpus luteum cystectomy or ovariectomy during the first trimester, the patient should

receive IM 17- $\alpha$  hydroxyprogesterone caproate 250 mg weekly for 4 weeks as progestogen support for the pregnancy [97].

#### 8.5.4.2 Bilateral Ovariectomy

In 1931, after removing both ovaries, the pregnancy continued [98]. The corpus luteum is indispensable to pregnancy for the first 2 months, and removal during that time precipitates abortion.

After removing a corpus luteum of early pregnancy (<12 weeks) or bilateral ovariectomy, progesterone replacement is advisable.

### 8.5.5 Adjuvant Chemotherapy

If the adnexal mass turns out to be ovarian cancer, the treatment is similar to that of the non-pregnant women depending on the stage, gestational age, and staging and grade of the



tumor [99]. In certain circumstances, it may be justified to remove the tumor only and await fetal maturation, while in some cases, chemotherapy may even be given while awaiting pulmonary maturation [4, 100].

## 8.6 Prognosis

### 8.6.1 Maternal Outcome

In Barrett's series in 1913, in which expectant tumor treatment was carried out, the maternal mortality was 18.4%, as against 2% in patients treated surgically [101]. Laparoscopy results in decreased length of hospital stay, less blood loss, and a lower incidence of postoperative complications [102].

#### 8.6.1.1 Continuation of Pregnancy

Several possible pathophysiologic mechanisms can interfere with the normal continuation of pregnancy. First, it is a hormonal influence. The problem could arise if bilateral adnexectomy/ovariectomy is performed. Fortunately, there are cases with further normal pregnancy after that procedure (see Sect. 8.5.4.2). Second, it obstructs labor or pregnancy with the tumor or uterus incarcerated in the pelvis. The third is a secondary infection of primary ovarian pathology. Graefe stated that ovarian cysts produce abortions or premature labor in 14–20% of cases.

#### 8.6.1.2 Malignant Tumors

In 21 reviewed cases by Jubb, the diagnosis was followed by immediate laparotomy and unilateral oophorectomy. Fourteen patients had no further treatment. In 33% of re-explored patients, no residual carcinoma was found. Unfortunately, there is no record of grading of the carcinoma, and follow-up was inadequate. Because of this, the figure for the 5-year survival rate of nearly 60% is unreliable [35]. Creasman et al. treated patients with stage IA ovarian carcinoma more radically with good results at 5 years. It would seem equally likely that the good survival rates reflected early diagnosis at routine antenatal examinations of patients. The sacrifice of the

pregnancy does not improve the maternal prognosis, and unilateral oophorectomy can be employed [40].

### 8.6.2 Fetal Outcome

#### 8.6.2.1 Fetal Morbidity

The laparoscopy and laparotomy do not differ concerning the fetal outcome—fetal weight, gestational age, growth restriction, infant survival, and fetal malformations [65, 100, 103, 104]. Preterm labor is reduced with laparoscopy by severalfold [6, 77, 87]. There is only one long-term follow-up (1–8 years) study, with 11 cases, and no evidence of developmental or physical abnormalities in children after acute but non-obstetrical laparoscopic surgery during pregnancy [105].

#### 8.6.2.2 Fetal Mortality

No significant differences in fetal outcomes exist between emergency laparotomy (fetal mortality 18%) and scheduled laparotomy (fetal mortality 23%) [9]. Non-emergent GLS adnexal mass operations during the second trimester were completed without fetal loss [106]. Fetal loss is the same with laparoscopy and laparotomy [6, 87].

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# Ruptured Ectopic Pregnancy

# 9

## Abstract

Ectopic pregnancy is one of the most common nonsurgical abdominal conditions during pregnancy. Unfortunately, most of these presentations are during early pregnancy when the conceptus is not developed for independent life and is also not “viable.” Preoperative and early diagnosis is common due to the specific clinical presentation and the routine use of  $\beta$ HCG for women of reproductive age presenting with pain in the lower abdomen. Both conservative and operative interventions are available and successful depending on the fetal status and severity of bleeding. The biggest diagnostic and therapeutic dilemmas arise in patients with heterotopic or advanced abdominal pregnancies. The clinician should always look for intrauterine pregnancy preoperatively, even when ectopic pregnancy is confirmed. Advanced abdominal pregnancy poses a real intraoperative problem due to adherence of the placenta to surrounding organs and tissues, and insisting on its complete removal can cause significant and sometimes unstoppable bleeding. Hepatic and splenic pregnancies are prone to severe bleeding due to the pronounced vascularity of these organs.

## 9.1 Ectopic Pregnancy in General

*If a woman with a child be bled, she will have an abortion, and this will be more likely to happen the larger the fetus*

(Hippocrates, 400 BC)

*If one is confronted with a pelvic condition that follows no rules and conforms to no standards, he should think of ectopic pregnancy and pelvic tuberculosis.*

(Howard Atwood Kelly)

### 9.1.1 Incidence

Ectopic pregnancy (EP) is the implantation of a fertilized egg outside the uterine endometrium. The rate of EP is constantly increasing. EPs quadrupled from 17,800 in 1970 to 88,000 in 1989 [1]. This is an increase from 4.5/1000 to 16.8/1000. In 1992, the USA EP rate was estimated at 1.97% of all pregnancies [2] and was rising [3]. Further increase was during 2006–2013 in the USA [4]. The prevalence of EP among women attending an emergency department with first-trimester bleeding, pain, or both ranges from 6% to 16% [5]. An EP occurs with seasonal variation and is most common in June and December [6]. The reason is unclear, but the reproduction is seasonal, depends on photoperiod and temperature, and varies with different latitudes.



9.1.2 Risk Factors

*If the egg is too big, or if the diameter of the tuba Fallopiana is too small, the egg stops and can get no farther but shoots forth and takes root there.*  
(Pierre Dionis, 1718)

The overall risk is approximately 1/200 pregnancies, but may be increased 20- to 100-fold in specific subsets of women [6]. Risk factors are presented in Table 9.1.

As many as 50% of Fallopian tubes removed because of an EP show prior inflammatory disease.

**Table 9.1** Risk factors for ectopic pregnancy [3, 7]

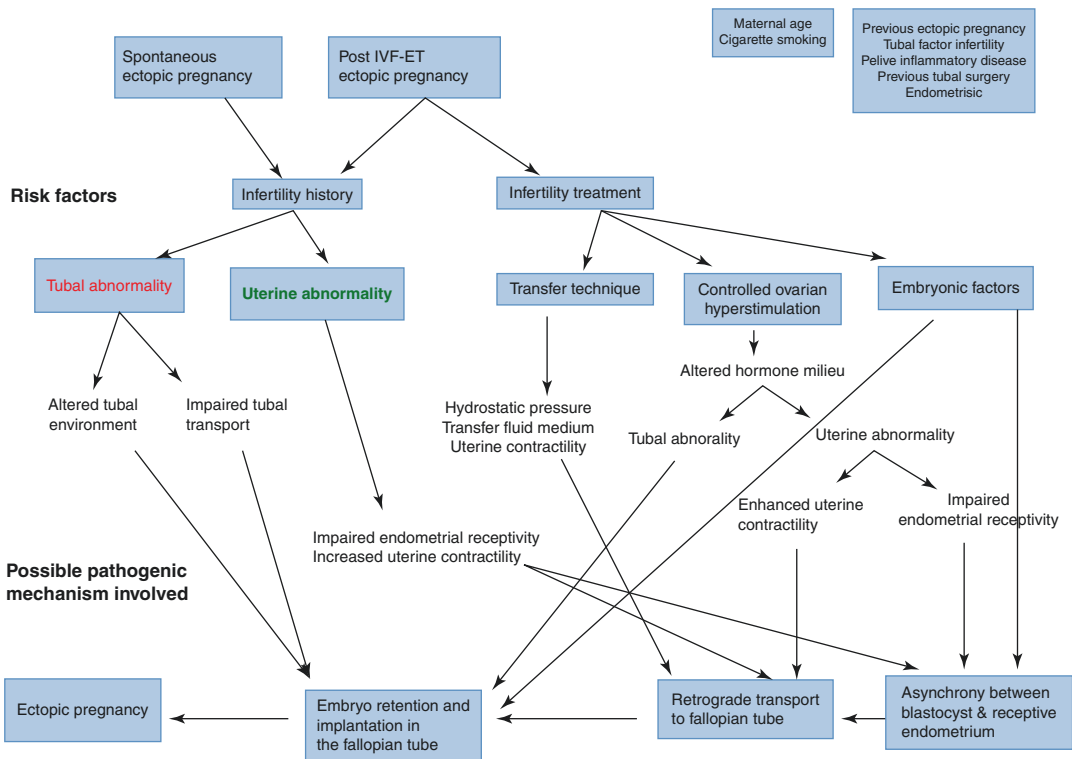
|                                                       |
|-------------------------------------------------------|
| Pelvic inflammatory disease                           |
| Previous tubal (ectopic) pregnancy                    |
| Current intrauterine device use                       |
| Previous tubal surgery, including tubal sterilization |
| Previous infertility treatments                       |
| Endometriosis                                         |
| Emergency contraception                               |

Although the risk of pregnancy is very low with a tubal ligation, if a pregnancy does occur, 10–50% are EP, representing a 20- to 100-fold increased risk [6]. Frequency is also higher with endometriosis, assisted reproductive technology (ART), and emergency contraception [7]. The pathogenesis of tubal pregnancy after natural and in vitro fertilization (IVF) conception is presented in Fig. 9.1.

9.1.3 Classification

9.1.3.1 Tubal Pregnancy

More than 95% of EPs implant the Fallopian tube. Pregnancies can grow in the fimbrial end (11%), the ampulla (70%), the isthmus (12%), and the cornual and interstitial part of the tube (2%) [9]. The tubal EP results from embryo retention within the Fallopian tube due to impaired embryo-tubal transport and alterations in the tubal environment allowing early implantation [10].



**Fig. 9.1** Potential mechanisms involved in the pathogenesis of tubal pregnancy after natural and IVF conception related to established risk factors. (Reproduced with permission from [8])



### 9.1.3.2 Non-tubal Ectopic Pregnancy

Less than 5% of EPs occur in the ovary, cervix, or intra-abdominally, and the locations slightly differ between normal conception and conception after ART (Fig. 9.2) [9].

### 9.1.3.3 Heterotopic Pregnancy

Heterotopic pregnancy (HP) is the coexistence of intrauterine and extrauterine gestation. The incidence of HP has been reported as 1/8000–1/30,000 in natural conception [12]. However, the rate is higher due to ART and is approximately 1/7000 overall and as high as 1/900 with ovulation induction [13, 14]. The Fallopian tube is the most common location with HP. However, cervical and ovarian HPs have also been reported [15, 16]. Most reported HPs are singleton intrauterine pregnancies. Triplet and quadruplet HPs are extremely rare [17, 18], frequently after ART.

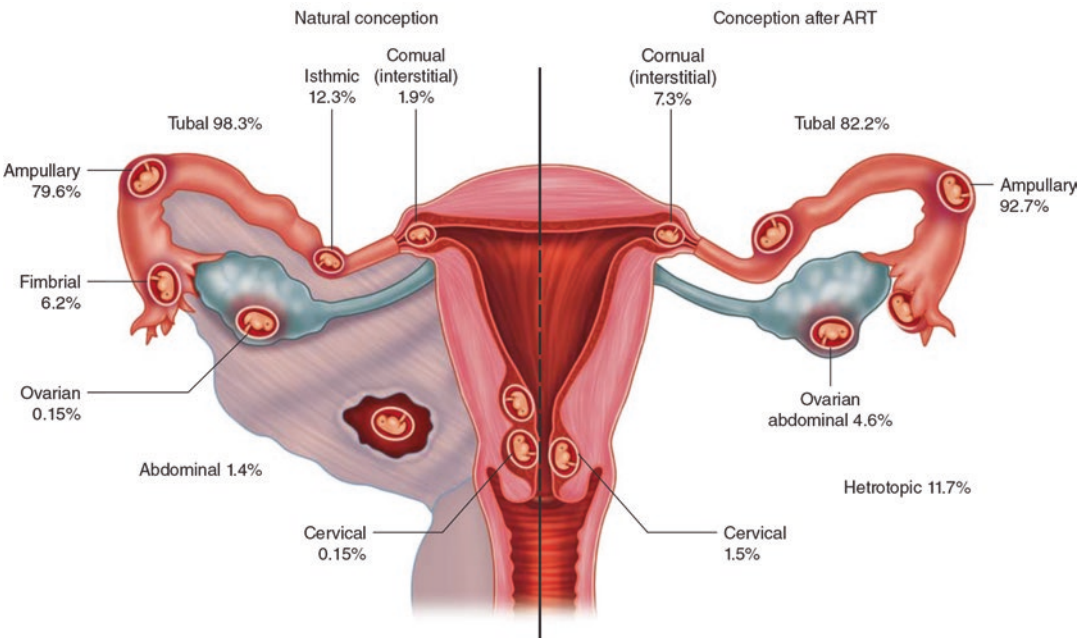
### 9.1.3.4 Persistent Ectopic Pregnancy

A persistent EP refers to the continuation of trophoblastic growth after a surgical intervention to remove an EP. After a conservative procedure to preserve the affected Fallopian tube, such as a sal-

pingotomy, some trophoblastic tissue, perhaps deeply embedded, has escaped removal and continues to grow, generating a new rise in  $\beta$ HCG levels [19]. After weeks, this may lead to new clinical symptoms, including bleeding. A less than 55% decline at day 3 predicts persistent EP and may select early cases for second-line methotrexate (MTX) therapy [20].  $\beta$ HCG dynamics in the week before salpingotomy and bleeding activity at surgery may identify patients at risk of persistent EP after laparoscopic linear salpingotomy [19].

### 9.1.4 Clinical Presentation

Textbooks from the first half of the twentieth century claimed that the diagnosis of EP was based on clinical criteria (gastric and mammary symptoms of pregnancy, cessation of the menstrual cycle, palpation of a tumor near an enlarged uterus, ballotement in the tumor, and purple discoloration of the vagina) and had 20% false pre-operative diagnosis of a ruptured EP. In contrast, diagnosing an unruptured EP was virtually impossible [21].



**Fig. 9.2** Sites and incidence of implantation in ectopic pregnancy following natural conception (*left*) and assisted reproductive technology (*right*). (Modified from [11])

#### 9.1.4.1 Medical History

The clinical features are complex and subject to significant variations in character and severity. A quote from Howard A. Kelly seems timely that *if one is confronted with a pelvic condition that follows no rules and conforms to no standards, he should think of ectopic pregnancy and pelvic tuberculosis* [22]. The explanation of these difficulties lies in the fact that the symptoms associated with extrauterine gestation arise not directly from the presence of the growing ovum in the Fallopian tube but from certain secondary lesions, either traumatic or inflammatory, which supervene. These *secondary lesions* may be briefly enumerated as follows [23]:

- intraperitoneal flooding from tubal abortion or rupture,
- intratubal bleeding leading to acute distension of the tube, the abdominal ostium being sealed,
- slowly progressive or recurrent bleeding leading to the formation of encysted collections of blood (pelvic hematoma, in the broad ligament, pelvic hematocele, in the pouch of Douglas, peritubal hematocele, around the abdominal end of the tube),
- infection of the gravid tube or an encysted collection of blood leading to suppuration.

Until these secondary lesions, extrauterine pregnancy gives no more local or general disturbance than an early pregnancy in the uterus. An important symptom associated with this phase, a brief period of amenorrhea, is the most helpful in diagnosis, but it is not always present. When a healthy adult woman, who is usually regular, goes for 2–3 weeks over the expected date of her period, there is a “strong presumption of pregnancy.” However, at this time, there is nothing to indicate whether the pregnancy is uterine or extrauterine. In the latter case, however, amenorrhea is of very brief duration, seldom more than 7–8 weeks, and then gives place to hemorrhage. In 30% of the cases, there is no amenorrhea at all. As it is quite unusual for an extrauterine gestation to continue undisturbed beyond the end of the second month, there is consequently no time for

the appearance of other general pregnancy symptoms. However, occasionally, morning sickness and early breast changes may be present.

When the course of the gestation becomes interrupted by any of the occurrences mentioned above, the clinical features undergo rapid transformation, and symptoms of extrauterine pregnancy appear—those that result from the interruption of the pregnancy by injury to the developing ovum or its containing sac. These symptoms, regarded as *secondary symptoms*, are highly variable in character and intensity in correspondence with the nature of the lesion which has given rise to them. The most easily recognized is *intraperitoneal flooding*; the symptoms that attend to it are uniform and characteristic. With a clinical history of amenorrhea and a careful pelvic examination made, mistakes are rare. Perforation of a hollow viscus, such as the stomach, duodenum, or gall bladder, is the only condition for which it is likely to be mistaken, even under the circumstances unfavorable for diagnosis. *Constant bleeding* from the uterus is a secondary symptom of extrauterine gestation. If no period of amenorrhea has occurred, it forms the initial symptom, and if there has been amenorrhea, it succeeds it. Mostly, it is the earliest indication of anything wrong. However, as the same thing frequently occurs from the disturbance of a uterine pregnancy, little importance is usually given to it. The bleeding is slight or moderate in degree, sometimes continuous, sometimes irregular; it is usually dark, thick, and syrupy in appearance. It may continue for several weeks if the patient is not relieved by the operation. The bleeding is due to separation and discharge of the uterine decidua, sometimes complete, more often in fragments. However, in most cases, the pieces of membrane do not attract attention. The most interesting phenomenon is this attempt on the uterus to throw off its decidua when the tubal ovum has been damaged. Some reflex mechanism is initiated, which excites uterine contraction insufficiently powerful to detach portions of the membrane from the uterine wall and gives rise to bleeding, which continues until the whole decidua has been expelled. It is possible that at the commencement, some blood that escapes

from the uterus may have made its way there from the gravid tube through the interstitial portion. In cases submitted to an operation, the hemorrhage always ceases a few days after removing the tube. Retained portions of decidua give rise to persistent bleeding.

The effects produced by the rapid effusion of a large quantity of blood into the peritoneal cavity are, in the order of their occurrence, as follows [23]:

1. acute abdominal pain,
2. fainting and the constitutional signs of bleeding,
3. shock, attended by vomiting and lasting for several hours.

No matter the nature of the secondary lesions with tubal pregnancy, two symptoms are common—uterine bleeding and pain. The pain has certain characteristics—sudden in onset, usually spontaneous, although muscular effort, such as lifting something heavy or the act of defecation, may appear to excite it. It is always severe and often most intense. First, it affects the whole abdomen. Later it may become localized. It is frequently attended with vomiting and signs of shock, sometimes with faintness or actual syncope; after lasting acutely for several hours, it subsides and may recur at varying intervals of a few days or a week until several attacks have been sustained; sometimes continuous pain without exacerbation follows the first attack. The initial pain attack is almost always due to bleeding; the subsequent attacks have a more complex origin. However, pain bearing the broad characteristics described above is a constant symptom of extrauterine gestation. In cases not immediately submitted to an operation, recurrent attacks of intense pain may occur from repeated intraperitoneal hemorrhages. The classic signs of hemoperitoneum except abdominal pain include shoulder pain caused by phrenic nerve irritation, an urge to defecate, and syncope, even in the absence of hypovolemia.

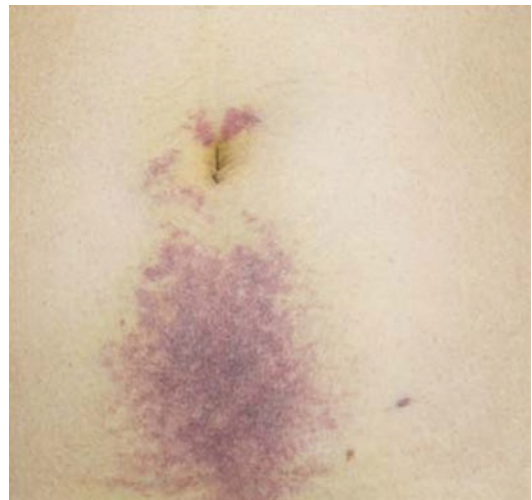
Rupture of ovarian pregnancy classically occurs during the first trimester and is preceded by pain corresponding to distension of the ovar-

ian capsule. In developed countries, due to early diagnosis, only 8–21% of ovarian pregnancies are observed with hemodynamic shock [24].

For *simultaneous intestinal obstruction with ectopic pregnancy*, see Sect. 18.12.2. Subjective symptoms of pregnancy may also be present, such as breast tenderness and emesis gravidarum.

#### 9.1.4.2 Physical Examination

*Cullen's sign* (Fig. 9.3) is the bluish-black appearance around the umbilicus, unassociated with any history of injury, and a definite uterine history usually typical of the slow tubal abortion type of bleeding. Although Cullen first described the sign in 1918 and labeled it a new sign in ruptured extrauterine pregnancy [26], discoloration of the umbilicus due to peritoneal extravasations had been previously reported by Ransohoff in 1906. He described jaundice of the umbilicus in a patient with a ruptured common bile duct. In 1909, Hofstatter observed a blue discoloration of an umbilical hernia (*Hofstatter's sign*) in a patient with a ruptured tubal gestation. However, the discoloration in Hofstatter's case was not due to ecchymosis, but rather the transmission of the



**Fig. 9.3** *Cullen's sign* is a bluish-black appearance around the umbilicus; extension does not depend on the amount of bleeding but the duration of the primary process and other undetermined factors. (Reproduced with permission from [25])

color of the blood through the thinned-out semi-transparent hernia.

Meyers et al., by computed tomography, first noted that blood in the abdominal wall might be responsible for these signs [27]. They defined the anatomy of various retroperitoneal spaces and compartments, revealing a direct extension of hemorrhagic fluid from the posterior pararenal space to the lateral edge of the quadratus lumborum muscle, where a defect in the transversalis fascia permits access to the abdominal wall musculature. The intramuscular hemorrhagic fluid presumably reaches the subcutaneous tissues via interruptions in muscular continuity. Cullen’s sign results from tracking blood along the round ligament to the umbilicus. The portal of entry to the round ligament complex from the retroperitoneum is via the gastrohepatic ligament to the falciform ligament at the inferior-posterior liver edge [28]. The falciform ligament contributes to the connective tissue tube covering the round ligament (obliterated left umbilical vein) as it passes to the umbilicus.

The appearance of periumbilical ecchymosis is a rare and late manifestation of intraperitoneal bleeding. In Cullen’s case, the discoloration began 1 week after the onset of pain. Undoubtedly, prompt surgical treatment prevents the development of that sign in many cases. It is possible that in some cases, the sign appears after the operation without being observed preoperatively. One also wonders how many patients with tubal abortion, who undergo spontaneous resolution without operation, may develop the sign and never come under medical observation. The presence or degree of discoloration is not related to the amount of bleeding but rather to its duration and other undetermined factors (Table 9.2).

Adnexal masses are often not palpable [29, 30], and tachycardia is not always present. Atypical findings include paradoxical bradycardia [31], fever [32], and uterine enlargement suggestive of an IUP [32]. Rectal bleeding is a sign of communication (infiltration) between colorectum and EP (see Sect. 26.6).

**Table 9.2** Conditions associated with non-iatrogenic Cullen’s sign

|                                |
|--------------------------------|
| Acute pancreatitis             |
| Pancreatic trauma              |
| Ruptured ectopic pregnancy     |
| Ruptured aortic/iliac aneurysm |
| Ruptured spleen                |
| Perirenal hematoma/bleeding    |
| Ruptured common bile duct      |
| Perforated duodenal ulcer      |
| Hepatocellular carcinoma       |
| Hepatic lymphoma               |
| Amebic liver abscess           |
| Metastatic thyroid cancer      |
| Rectus sheath hematoma         |

**9.1.5 Differential Diagnosis**

Differential diagnosis of Cullen’s sign includes several conditions. Periumbilical cellulitis typically causes blanching erythema that is warm to the touch. *Sister Mary Joseph’s sign* (nodule)—a metastatic spread of an intra-abdominal malignancy to the umbilicus—may present with thickening and erythema of periumbilical skin or as a palpable mass lesion around the umbilicus [33]. Subcutaneous administration of heparin may result in abdominal wall ecchymoses, which are typically distant from the umbilicus. Patients with psoriasis may develop periumbilical erythema with a silvery scale that bleeds on removal (*Auspitz’s sign*). Umbilical endometriosis is accompanied by bleeding in conjunction with the menstrual cycle. Ulceration of a recanalized umbilical vein in the setting of cirrhosis may cause periumbilical skin darkening [34].

Signs of intra-abdominal bleeding without Cullen’s sign have various nontraumatic causes.

**9.1.6 Diagnosis**

HP can have various presentations. Before symptoms, it is more likely: (1) with persistent or rising  $\beta$ -human chorionic gonadotropin ( $\beta$ HCG) levels after dilatation and curettage for an induced/spontaneous abortion, (2) when the uterine fundus is larger than for menstrual dates, and

(3) when more than one corpus luteum is present in a natural conception. There are two symptomatic presentations. One is when the intrauterine pregnancy (IUP) is discovered later than the EP, mainly because of the typical clinical presentation of EP before the woman is aware of the pregnancy. Another is abdominal pain/acute abdomen/hemoperitoneum/hemorrhagic shock in a woman with known early pregnancy. Difficulty in diagnosis in this second form is due to ultrasound (US) findings of normal IUP pregnancy and a rare incidence of additional EP.

#### 9.1.6.1 Laboratory Findings

The urine  $\beta$ HCG assay is sensitive to  $\leq 25$  mIU/mL, and more than 95% of patients with EPs have a positive test [35]. Transvaginal US has replaced transabdominal US for EP diagnosis and early screening of an IUP. It can visualize an intrauterine sac at an earlier gestational age. A gestational sac should always be seen in the patient with a viable IUP when the serum  $\beta$ HCG reaches 2000 mIU/mL. The gestational sac is usually visible at 1000 mIU/mL [36]. Following serum  $\beta$ HCG titer (which should double every 48 h in a normal, viable pregnancy) has no role in a patient with a suspected ruptured EP, as that patient needs immediate surgical attention. Depending on the severity of the bleeding, hemoglobin levels might be lowered or even normal [37]. Misleading and unexpected laboratory values such as hyperglycemia might also be present [38]. Diagnosis of an EP before rupture cannot always be obtained because the patient is unaware of the pregnancy. All women of childbearing age should have a pregnancy test performed regardless of the date of their last menstrual period. Among women with symptoms and inconclusive US assessments, the progesterone test (five studies with 1998 participants and cutoff values from 3.2 to 6 ng/mL) predicted a nonviable pregnancy with a pooled sensitivity of 74.6%, specificity of 98.4%, the positive likelihood ratio of 45 (7.1–289), and negative likelihood ratio of 0.26. The median prevalence of a nonviable pregnancy was 73.2%. The probability of a nonviable pregnancy was raised to 99.2% if the progesterone was low. For women with symptoms alone, the progester-

one test had a higher specificity when a threshold of 10 ng/mL was used and predicted a nonviable pregnancy with a pooled sensitivity of 66.5%, specificity of 96.3%, the positive likelihood ratio of 18 (7.2–45), and negative likelihood ratio of 0.35. The probability of a nonviable pregnancy was raised from 62.9% to 96.8% [39].

#### 9.1.6.2 Transabdominal Ultrasound

The US helps to exclude blighted ovum or threatened abortions. Transabdominal US of HP demonstrates free intraperitoneal fluid and a normal-looking IUP with a positive fetal heart rate. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of transabdominal US as a diagnostic modality in the evaluation of suspected EP were 73.1%, 75%, 95%, 30%, and 73.3%, respectively. In comparison, transvaginal US has 92.3% sensitivity, 75% specificity, 96% positive predictive value, 60% negative predictive value, and 90% accuracy [40].

*Ultrasound is the primary diagnostic modality, using a transvaginal approach supplemented by transabdominal imaging if required. (Royal College of Obstetricians & Gynaecologists, 2016 [41])*

#### 9.1.6.3 Transvaginal Ultrasound

Positive pregnancy test with abdominal pain mandates bedside US in the emergency department to locate the position of the fetal sac. The transvaginal technique is preferred because of its increased sensitivity for detecting an IUP and superior visualization of the adnexa [3]. Most patients with EPs have some abnormality on the US [42]. These abnormal findings include a cystic or complex adnexal mass (60–90%) and free fluid in the peritoneal cavity (25–35%, higher in a ruptured EP) and should raise the suspicion of EP. However, the findings are nonspecific, and not visualizing an EP on US can never exclude it as a possible diagnosis. Ectopic fetal heart activity location confirms EP [29]. There are pitfalls involved with overreliance on laboratory values



in evaluating EP. Serum  $\beta$ HCG above the “discriminatory” level (at which US should be able to detect an IUP) might lead to a diagnosis of EP when no IUP is visualized; however, values that fall below this level do not eliminate the emergent US. In many cases, US might nonetheless be diagnostic. Recently, a case was diagnosed with 3D US [42].

Since EPs are usually discovered and removed early in the pregnancy, an US may not find the additional pregnancy inside the uterus. When  $\beta$ HCG levels continue to rise after the removal of the EP, there is a chance that a pregnancy inside the uterus is still viable. This is usually discovered with an US.

The US criteria of a *cesarean scar pregnancy* include [43]: (1) an empty uterine cavity and cervical canal, (2) development of the gestational sac in the anterior portion of the lower uterine segment, and (3) absence of healthy myometrium between the bladder and the gestational sac.

IUP with hemorrhagic corpus luteum can simulate HP/EP clinically and on US [44]. Other acute abdominal conditions may simulate HP making clinical diagnosis challenging. Bicornuate uterus with gestation in both cavities simulates an HP. High-resolution transvaginal color Doppler US shows increased flow with a significantly reduced resistance index for the trophoblastic tissue in the adnexa from HP [13].

#### 9.1.6.4 Abdominal CT

An abdominal CT shows EP commonly as a ring-enhancing adnexal cystic mass surrounded by hemoperitoneum (Fig. 9.4).

#### 9.1.6.5 Abdominal MRI

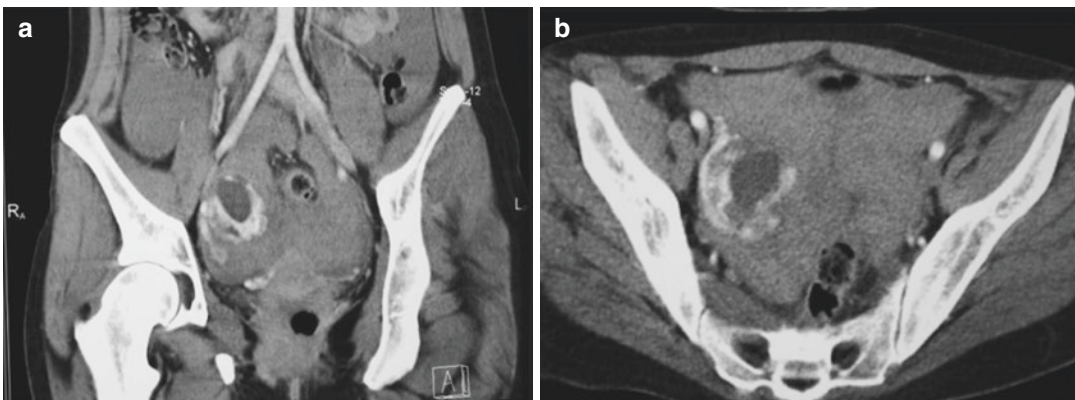
Cervical pregnancy, cervical abortion, and uterine scar pregnancy should be distinguished. If the 3D US is not available, MRI confirms cervical pregnancy, as tissue characterization is better with MRI, especially in doubtful cases [46]. The MRI findings of cervical pregnancy include [46]: (1) a mass with heterogeneous signal intensity and (2) partial or complete dark rim on T2-weighted images (Fig. 9.5).

MRI sensitivity, specificity, and accuracy for EP are up to 95%, 100%, and 96%, respectively.

#### 9.1.6.6 Culdocentesis

Culdocentesis may gain additional information. A needle is inserted through the vaginal wall into the posterior cul-de-sac with possible findings:

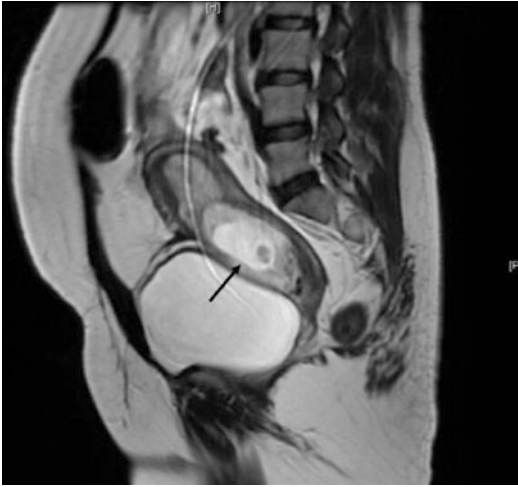
- a dry tap is inconclusive,
- a few cubic centimeters of clear fluid (peritoneal fluid) rule out a ruptured EP, but neither rule out an unruptured EP,
- a lightly bloody fluid (hematocrit <15) is inconclusive. This could be from a traumatic tap or early, mild bleeding from an EP,



**Fig. 9.4** (a) A coronal multiplanar reconstruction and (b) axial contrast-enhanced CT shows well-vascularized solid-cystic mass 45 × 40 mm, with a strong and early

peripheral contrast enhancement in the right adnexal area. (Reproduced with permission from [45])





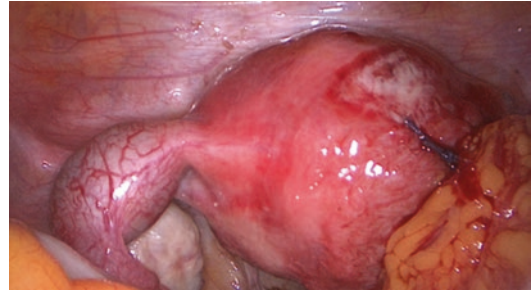
**Fig. 9.5** A coronal multiplanar T2-weighted MRI sagittal section of the pelvis shows a gestational sac with a fetal pole in the closed cervix (*arrow*) and hour-glass configuration of the uterus with thickened endometrium. (Reproduced with permission from [47] under the CC BY 3.0)

- moderately bloody fluid (hematocrit >15) indicates hemoperitoneum consistent with ruptured EP, but is nonspecific, and any internal bleeding (hemorrhagic ovarian cyst) can give this result,
- bright red, clotting blood usually indicates a traumatic tap or aspiration of blood from a vessel.

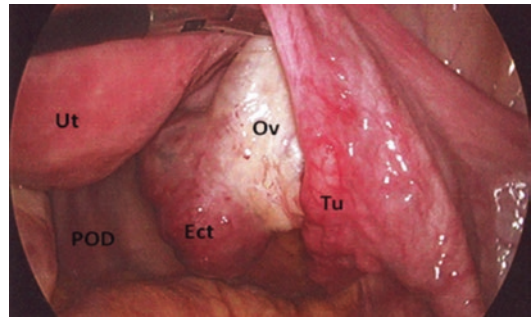
Today, it has lost its significance due to invasiveness, low specificity, and accuracy of abdominal CT. Approximately 50% with a positive culdocentesis have a ruptured Fallopian tube [48].

#### 9.1.6.7 Diagnostic Exploration

EP is commonly diagnosed during abdominal exploration (Fig. 9.6). Primary ovarian pregnancy is usually diagnosed at operation, although it may resemble a hemorrhagic corpus luteum cyst (Fig. 9.7). A correct intraoperative diagnosis was 28% [51]. Figure 9.8 shows recommended approaches to investigating first-trimester pain or bleeding in the hemodynamically stable patient.



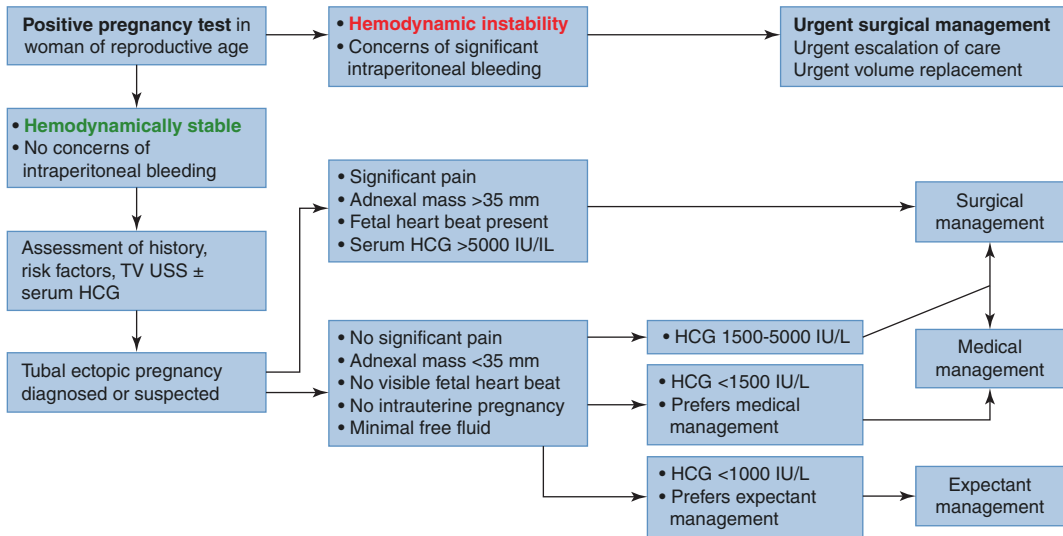
**Fig. 9.6** Laparoscopic view of a 30 × 20 mm unruptured left ampullary pregnancy. The intermediate portion of the Fallopian tube is distended and blue. (Reproduced with permission from [49] under the CC BY 4.0)



**Fig. 9.7** Laparoscopic view of an unruptured right ovarian pregnancy. *Ut* uterus, *POD* pouch of Douglas, *Ect* ectopic pregnancy, *Ov* right ovary, *Tu* Fallopian tube. (Reproduced with permission from [50] under the CC BY 3.0)

#### 9.1.7 Treatment

When the diagnosis of EP can be neither established nor excluded by a complete diagnostic workup, management depends upon many factors. The overall condition and stability of the patient, the availability of close follow-up care with an obstetrician/gynecologist, and the proximity of the patient to the hospital are important considerations for early discharge. Decisions regarding the disposition of such patients should be made with a consulting obstetrician/gynecologist, and in some cases, admission to the hospital or surgical exploration might be preferred option.



**Fig. 9.8** Recommended approach to investigating first-trimester pain or bleeding in the emergency department. *HCG* human chorionic gonadotropin, *TV USS* transvaginal ultrasonography. (Reproduced with permission from [52])

### 9.1.7.1 Historical Perspective

In 1849, Harbert of Louisville was the first to perform surgery early enough to stop fatal bleeding [53]. After several autopsies on women, Robert Lawson Tait in London recognized that appropriate dissection and ligation of bleeding vessels would be effective in treating EP. He successfully performed a laparotomy to ligate the broad ligament and removed a ruptured tube. By 1885, Tait had accumulated a relatively large number of successful cases of salpingectomies [54, 55].

Hunter Robb, in 1907, proved experimentally that a hemorrhage would cease in from 15 to 20 min. He also maintained that a woman who weighs 130 lb must lose 4 lb of blood before she succumbs from the bleeding. So large amounts of blood are rarely found in the free abdominal cavity during an operation or postmortem examination. Robb further contends that the sudden removal of a large quantity of recently accumulated fluid in the abdominal cavity before the vessels have had time to adapt themselves to the altered mechanical conditions is dangerous and may be followed by syncope. He maintained that patients in whom the bleeding wound is sufficient to cause death are rarely seen in time to be saved

by the operation. So long as there is reasonable evidence that an immediate operation may be the wrong procedure, we must hold our hands and leave something to nature [56]. Ralph Waldo, in 1910, at the *American Association of Obstetricians and Gynecologists* meeting, presented the results at Lebanon Hospital of the deferred operation for extrauterine pregnancy. He collected 81 cases, and 70% were brought into the hospital in profound shock. None of the patients were operated on unless they showed signs of recovery from the shock which followed the hemorrhage. It was argued that a woman suffering from a ruptured EP seldom, if ever, dies of the hemorrhage, but of the shock which usually follows the bleeding. If the patient is subjected to the additional shock of the operation, the chances of recovery are minimized.

In 1913, Hartmann's textbook stated, "every ectopic should be operated upon when diagnosed." Expectant management led to 86% of maternal mortality, while surgery saved 85% of women [57]. The introduction of asepsis, anesthesia, antibiotics, blood transfusions, and MTX saved the lives of many women with EP and eliminated the need for the operation in the selected group.

Robert B. Hope (USA), in 1937, suggested peritoneoscopy in diagnosing EP [58]. For 3 years, he assisted the American internist John C. Ruddock (1891–1964). Ruddock concentrated on cardiology in the 1920s. He was an active member of the American College of Cardiology and, in 1931, became president of the California Heart Association. Ruddock used the McCarthy cystoscope and presented his peritoneoscope in 1934.

#### 9.1.7.2 Medical Treatment

For *unruptured* tubal pregnancy, conservative therapy with maternal IM MTX injections is the method of choice, preventing severe complications in subsequent gestations [59]. Ovarian reserve and subsequent ART cycle outcomes (without a time-dependent effect) were reassuring after MTX for unruptured EP. No adverse impact of MTX was detected [60]. Close follow-up might be considered in consultation with the obstetrician/gynecologist [3]. Any location EP can be successfully treated with maternal IM MTX [61].

#### 9.1.7.3 Fallopian Tube Pregnancy

##### Fallopian Tube-Sparing Surgery

Tube-sparing surgery is accomplished by removing the EP from the Fallopian tube via linear salpingostomy by making an incision on the antimesenteric portion of the tube over the bulge of the EP, removing the pregnancy, achieving hemostasis, and allowing the tube to heal by secondary intention. There are no differences in subsequent spontaneous pregnancy rates, adhesion formations, or fistula formation with or without closure of the incision site [62, 63], but lead more often to recurrent ipsilateral EP site, bleeding, and persistent trophoblastic tissue [64]. Trophoblastic tissue persists in approximately 5% [65].

A fimbrial expression consists of “milking” the pregnancy out of the Fallopian tube. This technique probably should be reserved for EPs located at or very near the fimbria itself.

Postoperative  $\beta$ HCG measurements are mandatory.

##### Salpingectomy

Salpingectomy is the procedure of choice (1) if the woman has no desire for further pregnancies, (2) for hemostatic control of an attempted salpingostomy, or (3) if the Fallopian tube appears unsalvageable. Salpingectomy is the standard procedure for a hemodynamically unstable patient or a woman with infertility. In a subset of patients, it results in equivalent pregnancy rates and a decrease in recurrent EP [66].

##### Hemodynamically Unstable Patient

Hemodynamic instability requires emergency median laparotomy. Before the surgical intervention, ruptured EP might require vigorous and immediate resuscitation with fluids and blood products. Oxygen should be applied, and an emergent obstetric consultation obtained.

##### Laparoscopy

Laparotomy was gradually replaced by laparoscopy. First trimester pregnancies have been exposed to laparoscopy to rule out EP, allowing progress to term gestations [67].

Shapiro and Adler [68] reported laparoscopic salpingectomy using electrocoagulation followed by excision for an EP in 1973. Salpingotomy by laparoscopy was first reported using multiple punctures in 1980 [69]. DeCherney et al. in 1982 described linear salpingotomy with a cutting current [70]. A laparoscopy reduces morbidity, recovery, costs, and equivalent future fertility rates compared with laparotomy [71, 72].

Conservative (salpingotomy) or radical (salpingectomy) treatment in women who wish to preserve reproduction has long been debated. Salpingotomy does not improve time to spontaneous ongoing pregnancy and leads more often to persistent trophoblast when contralateral tubal pathology is absent [64].

In women with a desire for future pregnancies with a tubal EP in a solitary tube or the presence of contralateral tubal pathology, (laparoscopic) salpingotomy is the treatment of choice [73, 74].

Approximately 3% of early EPs are not visualized by laparoscopy. If a pregnancy has been previously determined to be nonviable by serum  $\beta$ HCG or an undesired pregnancy, endometrial sampling by suction curettage determines whether an IUP was present. If chorionic villi are obtained from the uterine cavity, a concurrent EP with IUP is unlikely. Sampling the endometrium with biopsy instruments is inadequate and should not be used.

#### 9.1.7.4 Cervical Pregnancy

If US measurements show no cardiac activity in clinically stable patients and the gestational period is <9 weeks, systemic MTX may be tried [75]. A gestational period >9 weeks with the presence of cardiac activity demonstrated on US in a clinically stable patient may require the addition of intra-amniotic potassium chloride in addition to systemic MTX [75]. Second or third-trimester diagnosis may warrant hysterectomy. Treatment options for bleeding are tamponade with a Foley balloon, large vessel ligation, or angiographic embolization. Hysterectomy is reserved for intractable bleeding [75]. Often, more than one method is used to terminate cervical pregnancy [75].

#### 9.1.7.5 (Incidental) Appendectomy

See Sect. 15.9.1.2.

### 9.1.8 Prognosis

While the number of EPs has increased, the death rate from this disorder has steadily declined. The mortality rate in 1952 in the USA was 2.4% [76], with an estimated 876 USA deaths between 1980 and 2007 [77]. Still, the maternal mortality rate in the USA ranged from 200 to 400/10,000 cases of EPs and accounted for 13% of all pregnancy-related deaths [2]. The decreased mortality rate is secondary to early detection and intervention. With the advent of conservative surgery, the emphasis on early diagnosis and increased awareness of this condition may be an important factor in further reducing the morbidity and mortality of EP.

Mortality of a tubal pregnancy at the isthmus or within the uterus (interstitial pregnancy) is higher as there is increased vascularity that may result more likely in sudden major internal bleeding.

The survival rate of the uterine fetus of an EP is around 70%. Successful pregnancies have been reported from a ruptured tubal pregnancy, continuing by the placenta implanting on abdominal organs or outside the uterus.

## 9.2 Ruptured Cornual Pregnancy

### 9.2.1 Definition

The rudimentary horn of a unicornuate uterus arises due to partial development of one uterine horn and incomplete fusion of the two Müllerian ducts. In more than 75% of cases of the unicornuate uterus, a contralateral rudimentary horn is present. Most rudimentary horns contain functional endometrium and do not communicate with the unicornuate uterus [78–80]. However, the rudimentary horn has been described in the literature under various terms, including *unicornuate uterus with rudimentary horn*, *uterus bicornis unicollis with rudimentary horn*, *uterus bicornis unicollis with atretic horn*, *uterus bicornis with accessory horn*, *Roberts' uterus*, and *hernia uterus inguinale*. This freedom of terminology makes an assessment of this condition more difficult.

Contrary to the *American Fertility Society* classification of uterine anomalies, rudimentary horns may occur without a corresponding unicornuate uterus. In the bicornuate uterus, if pregnancy occurs in the well-developed horn, it usually continues. A significantly increased uterine rupture risk exists when conception occurs in the rudimentary horn [81]. In contrast, others claim that all rudimentary horn pregnancies rupture [78]. Francois Mauriceau, in 1669, reported the first case of rudimentary horn rupture [82].

### 9.2.2 Incidence and Pathophysiology

Noncommunicating horns account for 70–92% of cases [78–80]. Pregnancy in a noncommunicating rudimentary horn has a reported incidence of 1/76,000–1/150,000 [78, 83], with more than 600 cases published [78–80, 84, 85]. Of all ruptures, 13% occur in the first, 67% in the second, and 20% in the third trimester [78]. There is no significant difference in rupture rates of communicating and noncommunicating horns (52% and 47%, respectively). Since 1900, 30% of pregnancies went to term, but from 1990 to 1999, this was reduced to 6% because of earlier detection and intervention [78]. Rupture of the uterine horn occurs because of the inability of the malformed uterus to expand with increasing gestational age. It occurs following the transperitoneal migration of sperm or fertilized ovum zygote [80]. Pregnancy in a rudimentary horn can rupture between 10 and 20 weeks of gestation with associated life-threatening bleeding [86] due to poorly developed musculature that cannot stretch. It is highly uncommon for such cases to result in a viable fetus as they often result in rupture of the horn before the third trimester [87]. Only 10% reach term, and the fetal salvage rate is 2% [88, 89]. Rupture occurs commonly because of underdevelopment, variable thickness, and poor distensibility of the myometrium and dysfunctional endometrium. Rudimentary horn pregnancy can be further complicated by placenta percreta due to the poorly developed musculature, scant decidualization, and small horn size, the reported incidence being 11.9% [90, 91] or by twin pregnancy [90].

Implantation in a rudimentary horn of a uterus has an exceptionally high risk of rupture ( $\leq 81\%$ ) associated with the induction of labor [92]. Sir Harold Beckwith Whitehouse (Fig. 9.9) first observed the phenomenon in 1912. The decision for labor induction in women with a congenital anomalous uterus, especially in cases of a previous CS, must be carefully considered, given the higher incidence of UR. Although the UR rate for unscarred anomalous uteri during pregnancy is increased relative to normal uteri, the precise increase in risk associated with the different types of uterine malformations remains uncertain.



**Fig. 9.9** Sir Harold Beckwith Whitehouse (26 October 1882, Tipton, Staffordshire—28 July 1943, London). He succeeded Thomas Wilson in 1921 as a senior gynecological surgeon at the General Hospital and in 1924 as professor of midwifery and diseases of women at the University of Birmingham, becoming the third holder of this combined chair, the gynecological component first held by Robert Lawson Tait. He was long interested in the British Red Cross Society, became president of the Birmingham branch in 1937 and, during the war, acting county director and controller in 1940. In 1913–1914, when only thirty, Whitehouse was a Hunterian professor at the Royal College of Surgeons, lecturing on uterine bleeding. (Reproduced with permission from [93])

### 9.2.3 Clinical Presentation

As rudimentary horn pregnancies are always associated with catastrophic outcomes, every effort should be made to diagnose them before pregnancy or early gestation. A detailed history during the first visit includes complaints of severe dysmenorrhea. However, the rudimentary horn may be underdeveloped, with nonfunctional endometrium and dysmenorrhea absent in 50% [79, 87]. The incidence of endometriosis in functional rudimentary horns is similar to the incidence in women with normal uteri ( $<15\%$ ) [78]. Müllerian anomalies are commonly associated with spinal, cloacal, and renal anomalies (45–



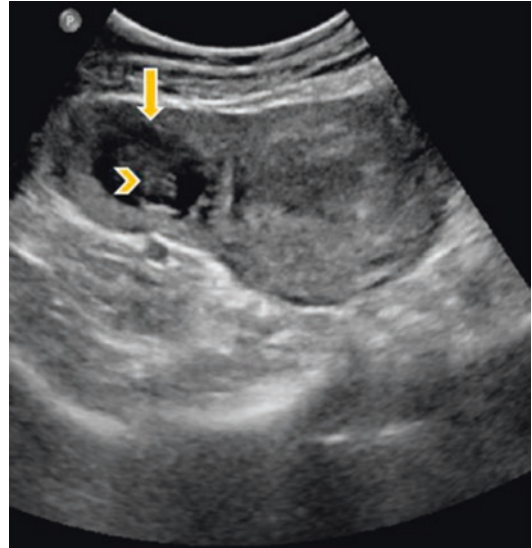
60%) [94–97]. The association of unilateral renal agenesis or ectopia, uterine duplication or unicornis, and vaginal agenesis has been described [98]. Unilateral renal agenesis predicts an ipsilateral obstructive Müllerian anomaly in 55–70% [99], but the reverse is not true. A significant rate (29–44%) of rudimentary horns is associated with abnormal renal anatomy [79]. The unicornuate uterus with a rudimentary horn may be associated with complications such as hematometra, endometriosis, infertility, recurrent miscarriages, preterm labor, malpresentation, and placenta accreta [100]. A possible explanation of complications is the noncommunicating horn in 70–90%, and fertilization is thought to occur by transperitoneal migration of gametes or in the pouch of Douglas. The most common reasons for hospitalization in women who were found later to have rudimentary horns were an EP (25%), chronic pelvic pain (20%), pelvic tumor (20%), and primary infertility (15%) [97].

A pelvic examination detects deviated uterus with a palpable adnexal mass causing deviation of the uterus and cervix to one side [101, 102], or a bicornuate uterus with the horns a wide distance apart should arouse suspicion of a Müllerian anomaly.

### 9.2.4 Diagnosis

Preclinical and preoperative detection of a rudimentary horn is persistently low (14% overall) [78]. The preclinical detection for obstetric presentations is 8%, which has not changed much (5–6%) since the 1960s [80, 97]. Diagnostic criteria for pregnancy in a rudimentary horn include [103]:

- Detection of a single interstitial tube in an empty uterus adjacent to the pregnancy,
- Free mobility and the presence of a vascular pedicle adjoining the gestational sac and the lateral aspect of the empty uterus.



**Fig. 9.10** US at the 7th week of pregnancy shows a bicornuate uterus with a gestational sac in the smaller right horn (arrow). The fetal pole is within the sac (arrow-head). (Reproduced with permission from [107] under the CC BY 4.0)

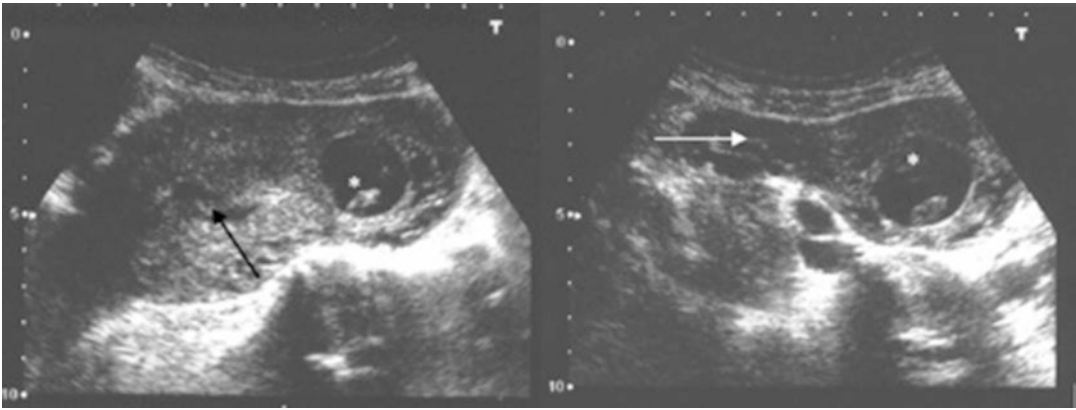
#### 9.2.4.1 Abdominal Ultrasound

The sensitivity of US for diagnosing rudimentary horn pregnancy is 30% [104, 105], with the first case of cornual pregnancy diagnosed with US in 1983 [106]. Previously stated criteria can be used with relative ease in the first trimester (Fig. 9.10), but as pregnancy progresses, it becomes more challenging to diagnose pregnancy in the rudimentary horn [108]. Furthermore, it is difficult to demonstrate the subtle anomalies associated with this condition. 3D US is useful in evaluating uterine anomalies [103, 104, 108]. Even cornual HP (Fig. 9.11) can be detected with transvaginal US [109].

#### 9.2.4.2 Hysterosalpingography

Hysterosalpingography can miss a noncommunicating uterine horn [110]. Diagnostic hysteroscopy may indicate a major midline malformation if tubal ostia are absent [111], although the procedure often needs to be done in conjunction with laparoscopy and dye studies. There is a high level of agreement between 3D US, hysterosalpingography, and laparoscopy in the classification of uterine morphology [112, 113]. The enlarging horn with thinned myometrium can obscure the





**Fig. 9.11** The image in the left panel shows an intrauterine gestation (*black arrow*) coexisting with an ectopic cornual pregnancy (\*) with a sac of 25 mm in diameter, containing an embryo with a crown-rump length of 13 mm. The image in the right panel shows the ectopic

pregnancy (\*) located in the right cornual region in continuity with the uterine cavity, in a funnel-shaped area in the upper uterine body that receives the insertion of the right Fallopian tube (*white arrow*). (Reproduced with permission from [109] under the CC BY 3.0)

adjacent anatomic structures, and the sensitivity decreases as the gestation increases.

#### 9.2.4.3 Abdominal CT

Abdominal CT or MRI is indicated if transabdominal or transvaginal US is equivocal in a stable patient. Free peritoneal fluid and the location of cornual pregnancy can be visualized (Fig. 9.12).

#### 9.2.4.4 Abdominal MRI

MRI accurately diagnoses pregnancy with a Müllerian anomaly and placenta percreta [114]. MRI can define a didelphys uterus with a fetus in one of the uterine bodies (Fig. 9.13). The placental invasion could remain elusive even with abdominal MRI and is diagnosed only at laparotomy [87]. Intraoperatively, an extrauterine pregnancy with a well-defined placenta differentiates a rudimentary horn pregnancy from an abdominal pregnancy because the placenta fits into the confines of the horn.

### 9.2.5 Treatment

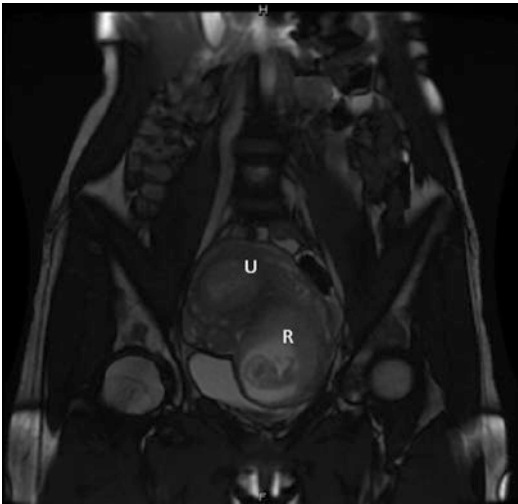
#### 9.2.5.1 Intra-Abdominal Access

Laparoscopic treatment of rudimentary horn pregnancy is increasing [115–117]. Though the



**Fig. 9.12** Abdominal CT (coronal section) shows a gravid uterus at the 7th week of pregnancy with a gestational sac towards the right side (*arrow*). A moderate amount of free fluid in the abdomen, especially around the liver (*arrowhead*). (Reproduced with permission from [107] under the CC BY 4.0)

gold standard for surgical management of hemodynamically stable women with EP, laparoscopy had long been considered a contraindication in



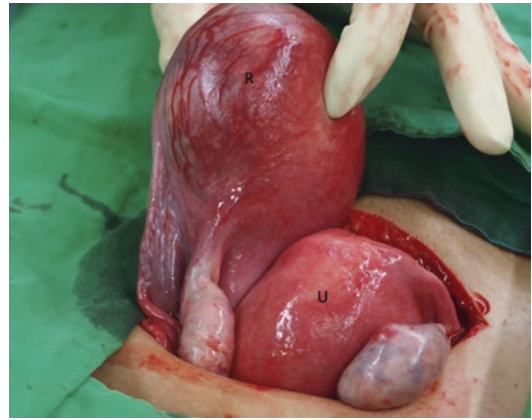
**Fig. 9.13** Abdominal MRI (T2 coronal view) shows the uterus (U) and the left rudimentary horn (R) pregnancy. (Reproduced with permission from [84] under the CC BY 4.0)

women with hypovolemic shock. There is always a concern of increased intra-abdominal pressure on the diaphragm and stomach, posing a significant threat to resuscitation and aspiration and pressure on the blood vessels, resulting in reduced cardiac output (see Chaps. 2 and 3). Most second-trimester rudimentary horn pregnancies have been managed by laparotomy [78, 80, 86, 118–120] with some exceptions [121]. The reason is more profuse bleeding from the enlarged uterus with hemorrhagic shock. Regardless of the intra-abdominal access, the fetus and the placenta should be removed.

#### 9.2.5.2 Procedures

##### Excision of Rudimentary Horn with Ipsilateral Salpingectomy

When diagnosed early, excision of the rudimentary horn with ipsilateral salpingectomy provides the best prognosis. It eliminates the remote possibility of EP due to transperitoneal migration of embryos [115, 122, 123]. Laparotomy is better (Fig. 9.14) for significant bleeding. In other cases, laparoscopy (Fig. 9.15) is advantageous. Tracking the course of the ureter on the side of the horn is essential to avoid accidental injury. Instilling vasopressin (20 IU/mL in a dilution of



**Fig. 9.14** Caudal view of the left noncommunicating horn (R) and the uterus (U) through Pfannenstiel incision. (Reproduced with permission from [84] under the CC BY 4.0)

1:60 with normal saline) at the horn's attachment site aids in hemostasis [121]. The attachment of the horn to the uterus can be divided by a medial or lateral approach, depending upon the type of attachment of the horn. A medial to lateral approach is preferred if the horn is attached to the uterus by a fibromuscular band [115]. Here, the uterine vessel medial to the horn is divided early in dissection, preventing excessive blood loss during surgery. The lateral to medial approach is utilized if the horn has a broad sessile attachment and the uterine vessel courses lateral to the horn. Electrocoagulation, harmonic scalpel, or stapling device can be used.

Even a spontaneous cornual rupture in the second trimester can undergo a direct repair of a defect closed in two layers with absorbable interrupted intracorporeal mattress sutures [121]. Pregnancy can continue under strict monitoring, followed by delivery via elective Cesarean section (CS) [125].

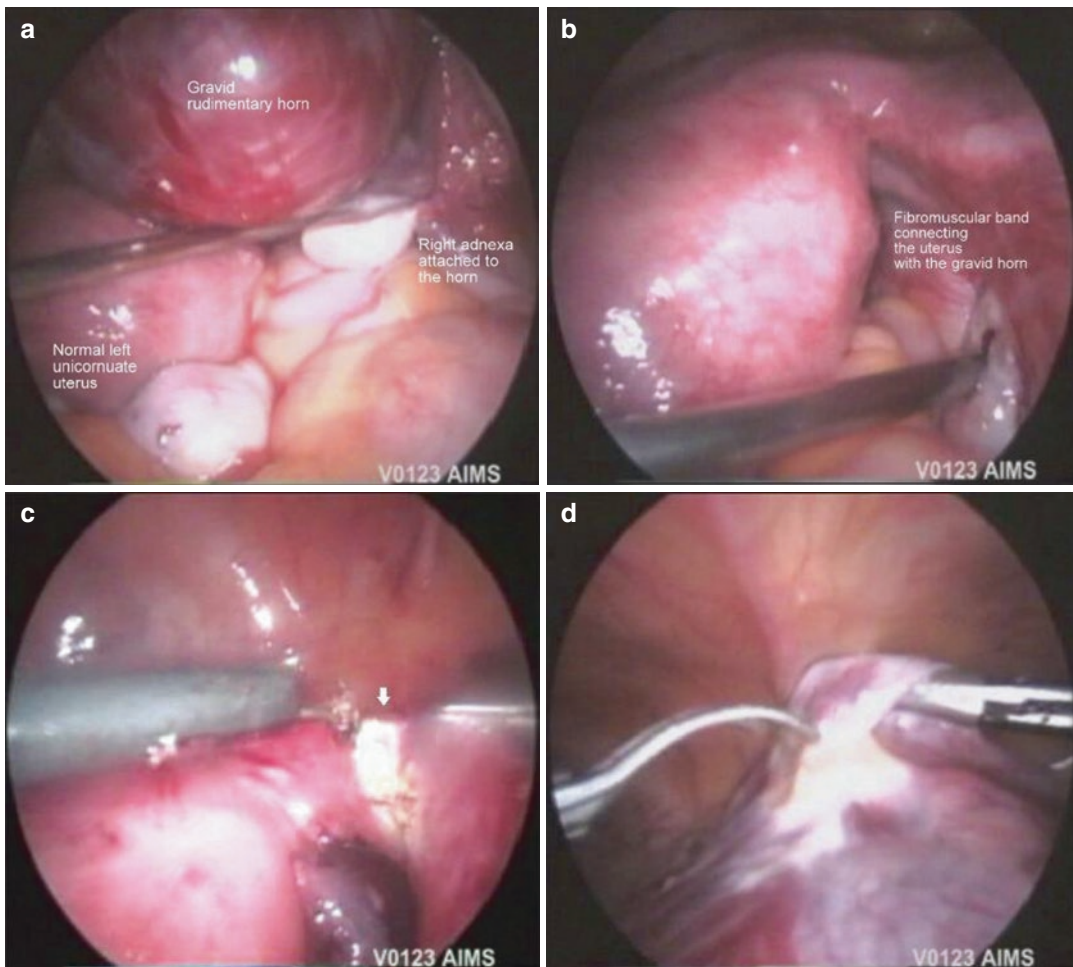
##### Cornuotomy and Cornual Resection

Laparoscopic cornuotomy yields similar clinical results as cornual resection. Laparoscopic cornuotomy may reduce operation time with a similar incidence of persistent interstitial pregnancy [126]. However, laparoscopic cornuotomy is sometimes combined with MTX therapy in ruptured EP complicated by persistent disease [127].

Before cornuotomy, diluted vasopressin (20 U in 60–100 mL of normal saline) is injected into the surrounding myometrium. An incision along the most bulging portion is performed with a monopolar current (Fig. 9.16a). Gestational tissue is evacuated with toothed forceps. Irrigation inside the incision is performed using high hydrostatic pressure. Bipolar cautery ensures hemostasis at bleeding sites inside the incision. Vertical mattress sutures (2-0 or 1-0 Vicryl) approximate the myometrium (Fig. 9.16b).

Variations of cornual resection exist. The most common is a deep circumferential incision

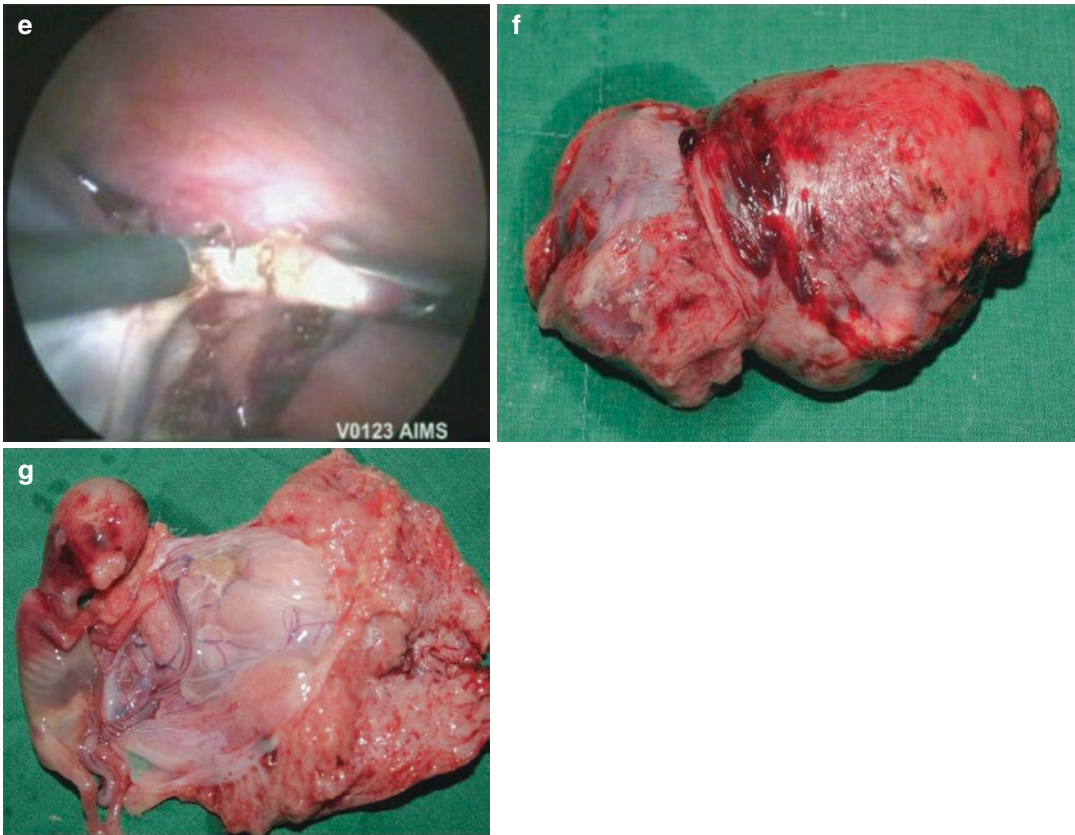
around the interstitial pregnancy followed by removal of the underlying myometrium and conceptual tissue. The second starts with a single linear incision cornuotomy. After removing the conceptual tissue, suspicious myometrium on both sides is excised at the base in an elliptical fashion. Extension of myometrium removal is based on the color and texture of the myometrium. The final variation also starts with a single linear incision cornuotomy. After removing the conceptual tissue, an endoscopic linear cutter stapler simultaneously removes suspicious myometrium and sutures. This technique is used when



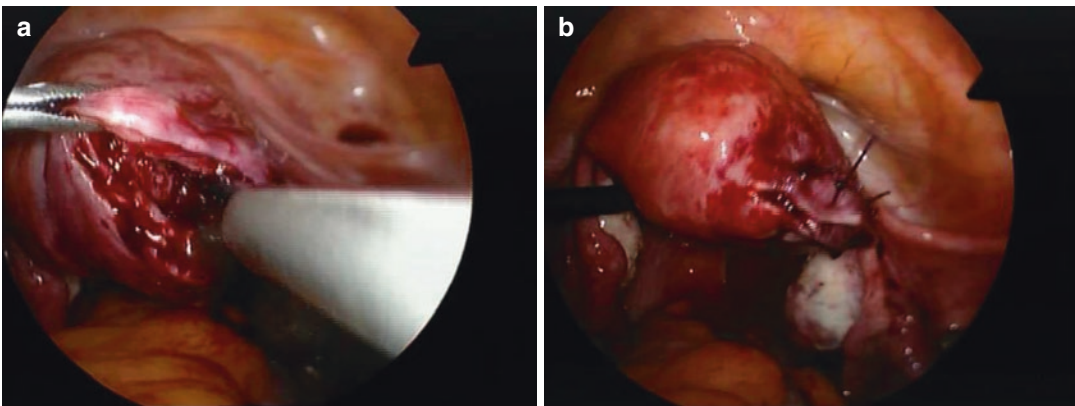
**Fig. 9.15** (a) Laparoscopic view showing anatomic relationships of the gravid rudimentary horn; (b) Fibromuscular attachment between the left unicornuate uterus and the pregnancy in the rudimentary horn; (c) Fibromuscular band being divided; (d) Lateral attach-

ments of the horn to round ligament; (e) Tubal attachment divided; (f) Intact specimen of rudimentary horn pregnancy; (g) Cut section of resected specimen. (Reproduced with permission from [124] under the CC BY 3.0)





**Fig. 9.15** (continued)

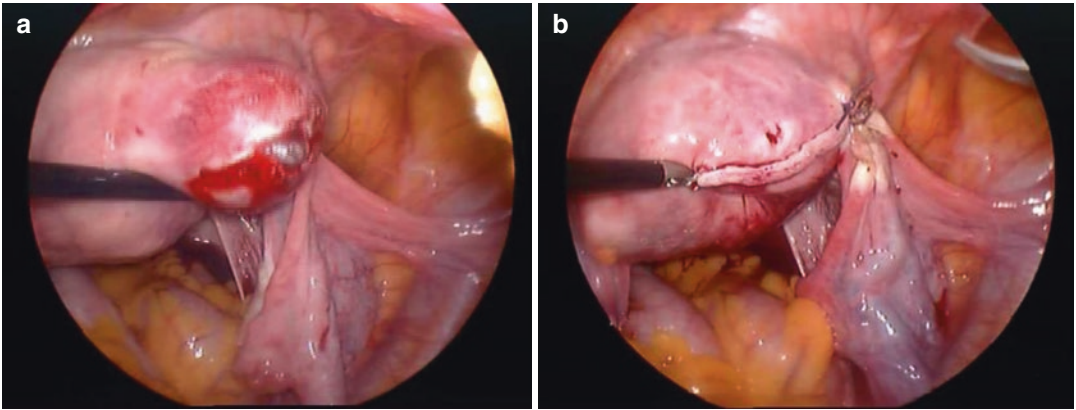


**Fig. 9.16** Cornuotomy procedure. (a) After a linear incision, the conceptual tissue is removed. (b) Incision is closed with a vertical mattress suture. (Reproduced with permission from [126])

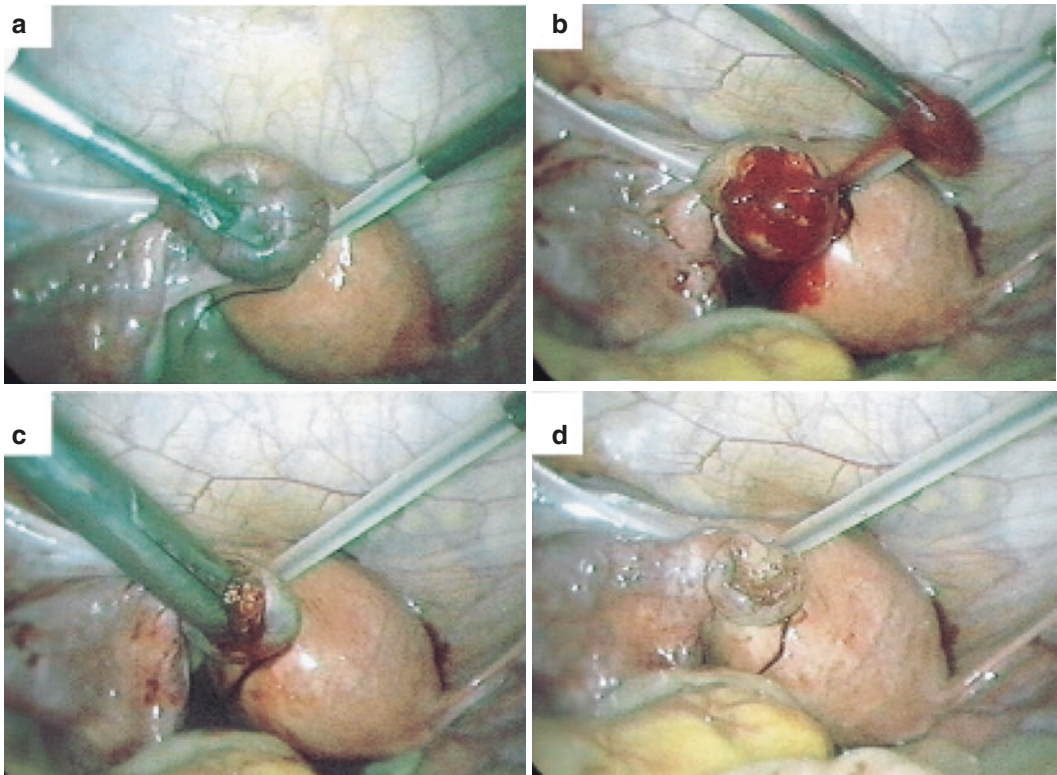
the bulging mass is small and superficially implanted (Fig. 9.17).

Uncontrollable bleeding during cornuotomy or cornual resection necessitates temporary or

permanent bleeding control methods. These include encircling sutures or placement of pre-formed knots around cornual pregnancy (Fig. 9.18) or temporary or permanent ligation or



**Fig. 9.17** Cornual resection procedure. (a) Mass is grasped with forceps, and the incision is along the bulge. (b) Myometrium is closed with the stapler. (Reproduced with permission from [126])



**Fig. 9.18** Endoloop placement before the evacuation of the conceptus. (a) After endoloop placement around the base of cornual pregnancy, the incision is made on cornu with tension kept on the endoloop. (b) A conceptus is

removed. (c) slightly increased density (*arrow*) compared to the liver parenchyma in (d) the venous phase that shows a non-enhanced. (Reproduced with permission from [128])

occlusion of the uterine artery or ascending branch of the uterine artery [129].

### Microsurgical Fallopian Tube Transposition

Elective microsurgical Fallopian tube transposition is recommended with a damaged contralateral tube [130, 131].

#### 9.2.5.3 Anesthetic and Perioperative Management

See Chap. 2. In nonurgent presentations, it is vital to evaluate the type of rudimentary horn and the possible presence of urological anomalies before embarking on the surgical excision to avoid associated complications [115]. Hence, the interval excision of the rudimentary horn after the complete preoperative evaluation is recommended [121, 132]. The rudimentary horn carries a risk for associated abnormalities. Therefore, an abdominal MRI should be performed after complete recovery, primarily due to the high risk of urinary tract anomalies [121].

#### 9.2.6 Prognosis

The mortality rate has been reduced from 23% at the turn of the twentieth century to 0.5% today due to earlier preoperative diagnosis and earlier intervention in ensuing hemorrhage.

## 9.3 Abdominal Pregnancy

### 9.3.1 Historical Perspective

The first reference to abdominal pregnancy is from the Talmud, in which rabbis reportedly observed a child who emerged from the abdominal side of the mother. Hindu legend states that Buddha was born through his mother's right side or armpit. The first reported abdominal pregnancy was by Abulcasis in the tenth century, who observed the discharge of fetal parts through the abdominal wall in the umbilical region. The first documented report of a successful abdominal pregnancy was in 1500 when a Swiss swine-gelder performed abdominal surgery on his wife.

Cornax described umbilical fistulae discharging fetal parts in 1545, Felix Platter in 1584, and Jacob Noierus in 1595. Both the mother and child survived. Walker von Solothurn, in 1887, made one of the first modern descriptions of this condition [133]. Galabin described the first case of primary abdominal pregnancy in 1896.

### 9.3.2 Classification

Abdominal pregnancies can be classified as *primary* when fertilization occurs outside the uterine adnexa or as *secondary* (thought to be more common), resulting from undetected rupture of early tubal pregnancy with subsequent implantation onto the peritoneal surfaces. In rare cases of uterine rupture (mostly rupture of a unicornuate or bicornuate uterus), the fetus may be extruded into the peritoneal cavity. At the same time, the placenta remains functional within the uterus, and the gestation continues as a uteroabdominal pregnancy. According to Studdiford's criteria, primary peritoneal pregnancy can be clinically distinguished from secondary peritoneal pregnancy (see Sect. 9.2.1).

Implantation can occur anywhere in the abdomen, including ligaments, liver, and spleen. Abdominal pregnancy is not strictly defined as *early* before 12–28 weeks of gestation and *advanced* after.

### 9.3.3 Incidence

Hellman and Simon from New York collected 316 reported cases from 1809 to 1935 [134]. They included a series of fetuses from 22 weeks' gestation to term. In 1935, the incidence was 1/9333 pregnancies [135].

The incidence varies widely with geographical location, the degree of antenatal attendance, the level of medical care, socioeconomic status, and different institutions in the same country [136–138]. It is presumed that abdominal pregnancy is more common in developing countries because of the high frequency of pelvic inflammatory disease with suboptimal treatment [139,



140]. Abdominal pregnancies make up a small percentage of EP [141]. Moreover, 98% of extra-uterine pregnancies are intratubal, 1% are ovarian, and the rest are primary or secondary peritoneal implantations. Atrash et al., in 1987, estimated the incidence of abdominal pregnancy at 10.9/100,000 live births and 9.2/1000 EPs in the USA [138] or between 1/3000 and 1/8000 deliveries in other studies [136, 137, 142, 143]. Ombelet et al. found an incidence of 1/402 pregnancies in developing countries and 1/10,000 pregnancies in developed countries [144]. Advanced abdominal pregnancy is rare and accounts for 1/25,000 pregnancies [145]. Until 2016, 28 cases of abdominal pregnancy after IVF were published [146].

### 9.3.4 Risk Factors

Risk factors include a history of tubal pregnancies, pelvic inflammatory disease, tubal sterilization, tubal infertility, tubal reconstructive surgery, endometriosis, transfer at the blastocyst stage, a higher number of embryos transferred, decreased endometrial thickness, variation in culture media, and fresh embryo transfer [8, 147–149]. Other women at risk include those who conceive despite using an intrauterine contraceptive device (IUCD) or progestagen-only contraceptive pills [150]. Without these risk factors, the undetected rupture of a tubal pregnancy is considered HP. Cocaine abuse increases the risk of abdominal pregnancy up to 20-fold [151]. Oehninger et al., in 1988, described the first case of abdominal pregnancy after IVF [152]. Mechanisms for abdominal pregnancy during IVF include [153]:

- uterine perforation during the transfer,
- spontaneous intra-abdominal fertilization,
- microfistula at the interstitial portion of the uterus.

### 9.3.5 Clinical Presentation

Diagnosis of HP/abdominal pregnancy is challenging. Even brilliant surgeons from the first

quarter of the twentieth century, such as Berkley, Bonney, Kelly, and Cullen, stated that they had made mistakes in diagnosing this condition. In 1936, preoperative diagnosis was 35% [154]. Clinical findings are extremely variable; today, preoperative diagnosis is unsuspected in up to 60% [155]. Sometimes it is found when abdominal exploration is indicated for other causes such as AA or tubo-ovarian abscess [156]. Spontaneous progression of undetected IUP from surgical management of acute or subacute ruptured EP on postoperative follow-up is rare. On the contrary, spontaneous abortion of an IUP has followed EP rupture [157].

Early diagnosis depends on the clinician having a high index of suspicion. Reece et al. defined four common symptoms and findings as follows [157]:

- Abdominal pain,
- Adnexal mass,
- Peritoneal irritation,
- Increase in uterine size.

Frequent signs and symptoms include crampy abdominal pain, vaginal spotting or bleeding, nausea, vomiting, malaise, and painful fetal movement [137, 142, 143, 155]. The most common physical findings are abdominal tenderness, an abnormal fetal position, and displacement of the cervix. Tal et al. reported abdominal pain in 83%, abdominal tenderness with hypovolemic shock in 13% of the HPs, and vaginal bleeding in 50%. Vaginal bleeding common with EP is rare in HPs because of the intact endometrium of IUP [158]. When the fetus dies, it will cause the cessation of all signs of pregnancy, such as enlargement of the breasts, etc. [159].

### 9.3.6 Diagnosis

In the USA, up to 1987, only one of nine women who reached the hospital alive had an accurate preoperative diagnosis of abdominal pregnancy [138].

### 9.3.6.1 Laboratory Findings

Laboratory tests such as abnormally increasing  $\beta$ HCG are not sufficiently reliable for the diagnosis, as are signs and symptoms such as abdominal pain and tenderness, persistent transverse or oblique lie, and palpable fetal parts [141]. Quantitative measurements of serum  $\beta$ HCG levels are of no use because the IUP will be producing normal and increasing levels of serum  $\beta$ HCG [160]. The absence of uterine contractions during oxytocin challenge testing suggests abdominal pregnancy [137].

### 9.3.6.2 Transabdominal Ultrasound

When coupled with clinical evaluation, transabdominal US (Figs. 9.19 and 9.20) has a 50–75% success rate [141]. US findings of abdominal pregnancy are as follows [162, 163]:

- demonstration of a fetus in a gestational sac outside the uterus or the depiction of an abdominal or pelvic mass identifiable as the uterus separate from the fetus,
- failure to see a uterine wall between the fetus and urinary bladder,
- recognition of a close approximation of the fetus to the maternal abdominal wall,
- localization of the placenta outside the confines of the uterine cavity.

The most frequent and reliable finding is a separation of the uterus from the fetus (90%).



**Fig. 9.19** Transabdominal US: pregnancy outside of the uterus. (Reproduced with permission from [161])

Extrauterine placenta (75%) and oligohydramnios (45%) are next in frequency. Other features include fetal parts close to the maternal abdominal wall (25%), failure to visualize myometrium between the fetus or placenta and maternal bladder (15%), abnormal fetal lie (25%), poor visualization of the placenta (25%), and maternal bowel gas impeding fetal visualization (25%) [163]. Clear identification of an empty uterus as a separate structure is essential for the diagnosis. This can be accomplished by giving close attention to the lower pelvis to ensure continuity between normally appearing vaginal and endometrial echoes. Findings that mimic abdominal pregnancy include pregnancy in a bicornuate uterus, pedunculated uterine fibroids associated with a gravid uterus, and a normal early pregnancy in a sharply retroflexed or anteverted uterus.

### 9.3.6.3 Abdominal MRI

An MRI confirms abdominal pregnancy, showing the same characteristics as abdominal US (Fig. 9.20) with a more precise definition of the location of the placenta and placental invasion of the surrounding structures (Fig. 9.21).

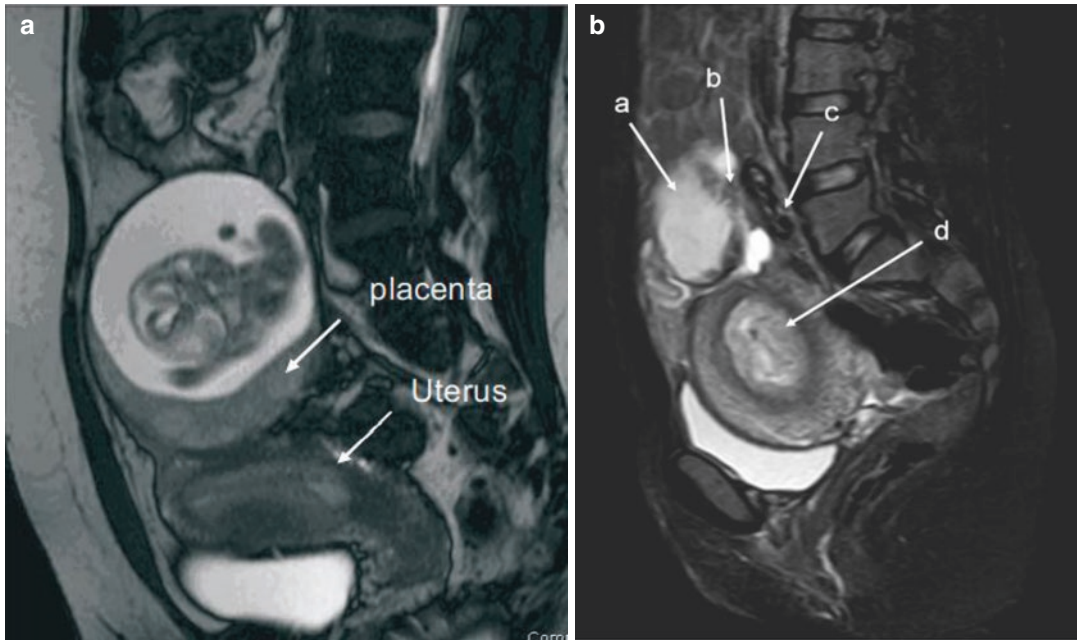
### 9.3.7 Treatment

*The effort to separate the placenta is attended with a great risk of fatal hemorrhage.*

(Edward Parker Davis, 1904)



**Fig. 9.20** Abdominal pregnancy: live fetus at 17 weeks with normal amniotic fluid. (Reproduced with permission from [161])



**Fig. 9.21** (a) MRI of abdominal pregnancy—the placenta is inserted on the posterior wall of the uterus. (Reproduced with permission from [161]). (b) T2-weighted sagittal MRI of the lower abdomen demon-

strating the placental invasion. Placenta (a), invasion area (b), sigmoid colon (c), uterine cavity (d). (Reproduced with permission from [164] under the CC BY 3.0)

Management depends on maternal hemodynamic status, congenital fetal abnormality, fetal viability, gestational age at presentation, and the availability of neonatal facilities. Surgical intervention is indicated with a dead fetus due to the risk of infection and disseminated intravascular coagulation. Some recommend 3–8 weeks of observation to allow atrophy of placental vessels [165]. If the diagnosis is uncertain and EP/abdominal pregnancy is suspected, laparoscopy can be diagnostic and therapeutic (Fig. 9.22).

#### 9.3.7.1 Conservative Treatment

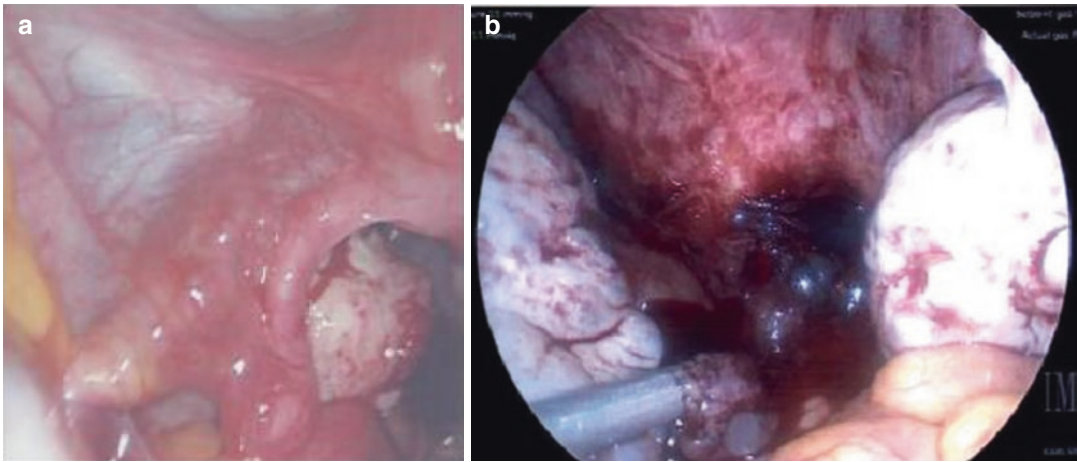
Sole treatment with MTX is ineffective in abdominal pregnancy with an embryo [167], but is added to surgical treatment [168]. Preoperative MTX treatment minimizes blood loss during surgery and facilitates maximal placental removal [169]. Because of the risks of placental separation, surgical intervention should immediately follow the confirmed diagnosis of abdominal pregnancy, regardless of the fetal condition [138].

However, in some circumstances, it could be possible to await fetal maturity [168].

#### >20 Weeks Gestation

If a conservative approach is considered for abdominal pregnancy at >20 weeks' gestation, the following prerequisites have been proposed [170, 171]:

- the absence of fetal malformation,
- the absence of maternal or fetal decompensation,
- continued surveillance of fetal well-being,
- placental implantation low in the abdomen, far away from the liver or spleen,
- adequate amniotic fluid,
- continuous hospitalization in an appropriate facility,
- informed consent from the patient.



**Fig. 9.22** (a) A reddish and edematous mass on the left infundibulopelvic ligament of early abdominal pregnancy. (Reproduced with permission from [166] under the CC BY

3.0). (b) Products of conception implanted in the posterior cuć-de-sac after intrauterine embryo transfer. (Reproduced with permission from [146] under the CC BY 4.0)

Maternal surveillance comprises physical examinations, serial US assessments, measurement of fetal growth, and daily fetal heart rate monitoring. Laparotomy can be planned for 34 weeks' gestation without complications.

### <20 Weeks Gestation

Continuing the pregnancy should be exceptional when the diagnosis is before 20 weeks of gestation. The importance of informed consent is paramount [168].

### 9.3.7.2 Surgical Treatment

If the fetus is alive, laparotomy should be performed regardless of gestational age or fetal condition [138, 139]. The reason is mainly based on the unpredictability of placental separation and consequential massive hemorrhage.

### Perioperative Embolization

Embolization of the placental vascular supply can be performed before surgery to minimize blood loss, during surgery to facilitate maximal placental removal [172–174], and after surgery to stop post-

operative bleeding [175]. Removal of an abdominal pregnancy by laparoscopy after embolization has been described [173]. Although no consensus regarding the treatment of the placenta in abdominal pregnancy has been established, most authors advocate leaving the placenta in situ unless the surgeon can be confidently assured that the entire blood supply to the placental bed can be surgically ligated without loss of excessive amounts of blood and the need for extensive blood replacement therapy. Unfortunately, if left in the abdominal cavity, the placenta commonly causes complications in the form of infection, abscesses, adhesions, intestinal obstruction, and wound dehiscence.

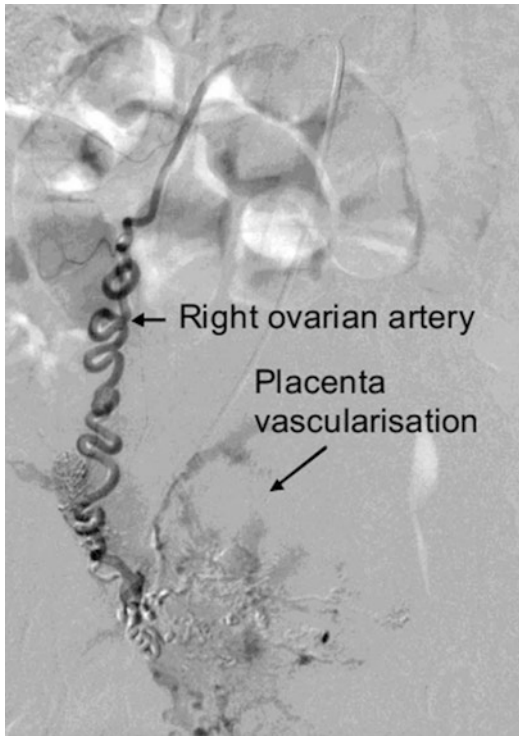
Preoperatively, the primary task is to identify all sources of blood supply to the placenta (Fig. 9.23) and to embolize vessels that could be difficult to ligate, such as the hypogastric artery. Another option is MTX administration to inactivate the trophoblast when the placenta has been left in situ [176]. It should be used before operation if fetal death is confirmed.

Routine angiographic evaluation includes abdominal aortography with renal, celiac, superior mesenteric, and internal iliac arteriography.

### Operative Procedure

Laparotomy should be performed through a mid-line incision [141]. It is advisable to make the





**Fig. 9.23** Catheterization of the right ovarian artery, which supplied the placenta in abdominal pregnancy. (Reproduced with permission from [161])

incision in the amniotic sac as far as possible from the placental attachment and large enough to extricate the fetus without trauma and permit the subsequent drainage of amniotic fluid [170]. Because of the high risk of bleeding, leaving the placenta in place is preferable by ligating the umbilical cord at its base. There is no effective method of controlling bleeding in the placental bed by clamping or cautery. Prolonged pressure, hot packs, and topical thrombin-containing compresses have been used with variable success. Using temporary aortic compression or an abdominal balloon pressure pack in the pelvis can be life-saving [170]. Leaving a drainage tube in place should be avoided, as this increases the risk of abscess formation and septicemia [177]. Nevertheless, it is ideal to remove the placenta if its blood supply can be secured, if the diagnosis is made early in pregnancy, or in cases with the fetal demise of more than 4 weeks' duration [178]. In these circumstances, removing the pla-



**Fig. 9.24** Fetus and placenta attached to the sigmoid colon (see Fig. 9.21b). (Reproduced with permission from [164] under the CC BY 3.0)

centa has been followed by fewer complications, less need for repeat surgery, and fewer repeat hospitalizations [179, 180]. In fact, placental removal has been associated with low morbidity but high mortality [181]. The actual procedure consists of an initial ligation of the placental blood supply and, afterward, the removal because massive life-threatening bleeding can occur due to the absence of a contracting uterus, which generally would occlude the placental bed [182]. Other treatment options regarding the placenta include partial removal or leaving the placenta in situ. In the case of partial removal of the placenta, a complete blood supply ligation is needed. If not, massive uncontrollable bleeding may occur [167]. Leaving the placenta in situ with the umbilical cord ligation can be associated with expectant management or other measures, which can accelerate placental trophoblast involution like MTX therapy or embolization [155, 172]. If the placenta is not removed completely, it has been estimated that the remnant can remain functional for approximately 50 days after the operation. Total regression of placental function is usually complete within 4 months [183].

Some have advised delay to allow the fetus to die and the placenta to become partly separated. When the fetus has been removed and the placenta found to be firmly attached to the bowel (Fig. 9.24), the membranes should be stitched to the abdominal wall and the placenta allowed to



remain while the amniotic sac is packed with sterile gauze. The pressure prevents bleeding, and the placenta gradually becomes loose, sometimes piecemeal and sometimes almost entirely.

If the organ to which the placenta is attached is removable, then the placenta should be removed together with that organ [184]. In cases where placental implantation has occurred in vascular areas such as the mesentery and vital organs, it has been recommended that the placenta should be left in situ because surgical excision can result in uncontrollable and life-threatening bleeding [185]. If discovery is not made until attempted CS, a safer alternative would be to defer delivery if possible, close the abdominal incision, and transfer the woman to an appropriate hospital. This could be done even after fetal delivery with the placenta left in situ if there is no bleeding [169].

Intraoperative steps of the abdominal wall and attachment to the uterus are presented in Fig. 9.25.

### Postoperative Management

Patients remain in intensive care for 24–72 h postoperatively. Complications could occur for several weeks. A retained placenta can persist in situ for several weeks and has remained detectable for 5 years [170].

Postoperative MTX use expedites placental absorption. However, its use is controversial. It might increase infective complications from rapid tissue necrosis, while some authors argue for complete placental regression. MTX as a folate antagonist causes an acute intracellular deficiency of folate coenzymes, thus affecting the synthesis of DNA, especially in rapidly multiplying cells. MTX acts on rapidly dividing cells, likely with limited effects on the mature placenta with its limited proliferative activity. With or without its utilization, the retained placenta will frequently undergo suppuration and require sur-

gical removal [155, 173]. Risks of secondary hemorrhage could be diminished while keeping the infection risk low. A case of placental infusion with MTX via the umbilical arteries has also been described [187]. Its use preoperatively, or actinomycin D, has been proposed to destroy trophoblastic activity with established fetal death [188].

## 9.3.8 Prognosis

### 9.3.8.1 Maternal Outcome

Maternal mortality ranges from 0.5% to 30% [136, 138, 142, 170]. From 1809 to the 1970s, it was 18.2% [189], principally from massive bleeding from incomplete or entire placental separation during the pregnancy (see Sect. 9.3.7.2). The mortality rate of abdominal pregnancy is sevenfold higher than that of a non-abdominal EP [138].

### 9.3.8.2 Fetal Outcome

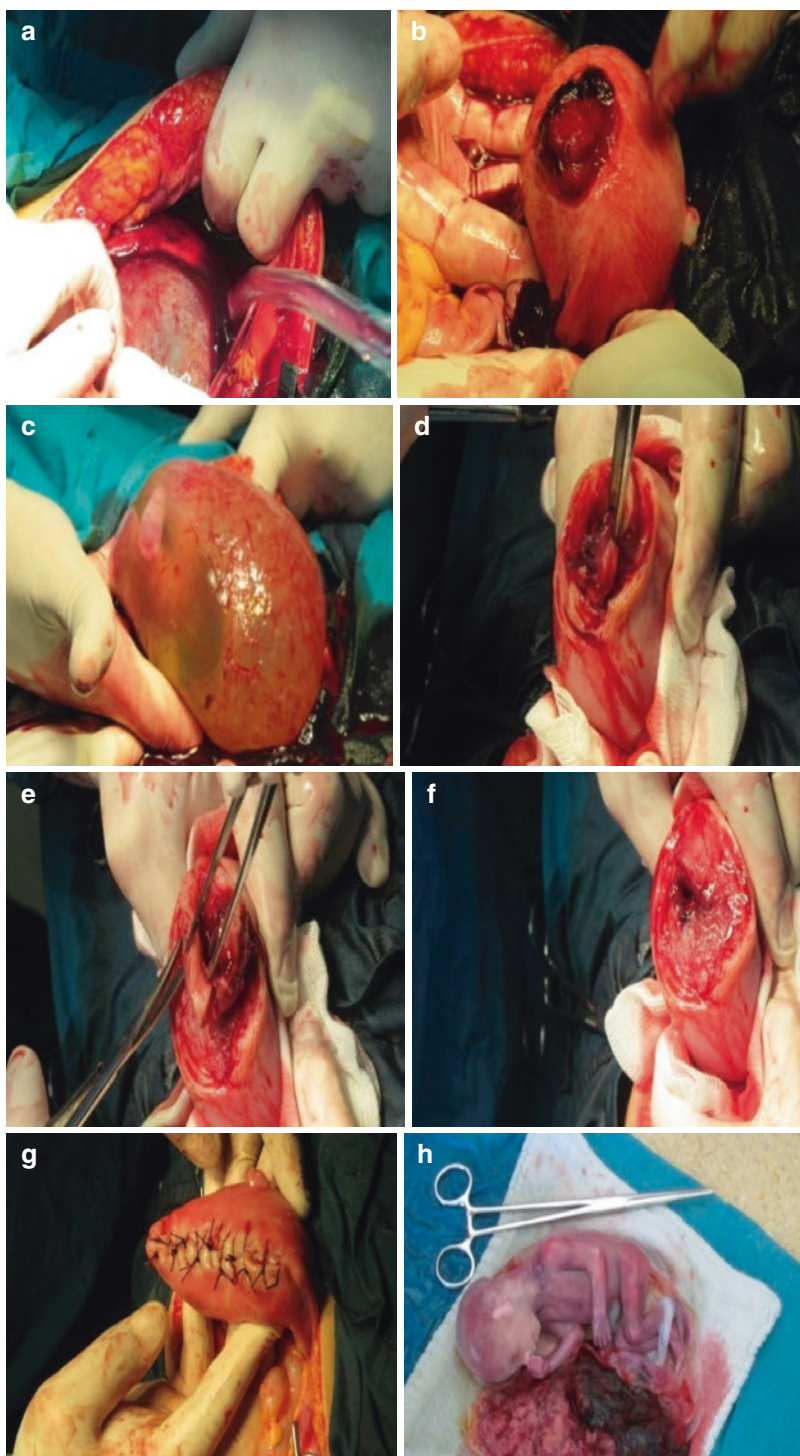
#### Mortality

The fetal outcome is poorer than the maternal outcome. The perinatal mortality is 40–95% [171, 190]. Through a survey of the literature from 1809 to 1919 and questionnaires from 200 obstetricians, Beck collected only 262 cases of extrauterine pregnancy after the fifth month with a living infant.

#### Morbidity/Deformations

Fetal abnormalities (congenital malformations) range from 20–40% to 90%, primarily from associated oligohydramnios [190]. Early amnion rupture can explain the band-related defects, the compression-related defects, or its combination [191]. With the fetus surrounded by an average amniotic fluid volume in advanced pregnancy, the fetal outcome tends to be better [170].

**Fig. 9.25** (a) The gestational sac is in direct contact with the anterior wall; (b) placental implantation site; (c) the gestational sac; (d) fundal uterine wedge resection; (e) elimination of the placental villi; (f) the excised fundal myometrium before applying sutures; (g) mattress sutures of the excised fundal myometrium; (h) the excised placenta and the fetus. (Reproduced with permission from [186] under the CC Attribution License)



## 9.4 Primary Hepatic Pregnancy

### 9.4.1 Historical Perspective

Cornell and Lash, in 1933, collected records of 236 pregnancies involving placental attachment to 641 sites, the great majority being in the pelvis. In eight cases, one attachment site was the liver, but the note was not made whether this was the sole area [192], probably meaning abdominal and not primary hepatic pregnancy. Chester M Echols in 1934 [193] and ME Barrett in 1952 [194] mentioned patients with the placental site on several organs, one of which was the liver, but these cannot be termed primary hepatic pregnancies. Billington and Goodchild in 1948 [195], Serebryakova and Kanshin in 1952 [196], Van de Loo in 1952, AHG Murley in 1956 [197], and Norman G. Kirby in 1969 [198] described the liver as the only placental site. Mear et al., in 1965, described a full-term living infant delivered at laparotomy (died after 45 min), but the mother died after further severe bleeding from the liver [199]. Luwiliza-Kirunda reported a lithopedion from a hepatic pregnancy in 1978 [200].

### 9.4.2 Incidence

Primary hepatic pregnancy is extremely rare. Since 1956, there have been approximately 60 cases published [201–203]. The median age of onset was 29.2 years (18–46 years) [202].

### 9.4.3 Risk Factors and Pathophysiology

Risk factors for any location EP are similar and listed in Table 9.1 [203]. An additional risk factor is perihepatic adhesions from ascending pelvic inflammatory disease entrapping fertilized eggs [204].

The liver and the spleen are favorable for implantation because they are flat organs, rich in blood flow, and easily reached by the fertilized ovum [205]. However, both cannot allow placental attachment, resulting in rupture with massive hemoperitoneum [206]. Still, there is a significant difference in bleeding incidence between splenic

and hepatic pregnancy. Most splenic pregnancies become symptomatic, commonly as bleeding up to 8 weeks of pregnancy (see Sect. 24.2). On the contrary, hepatic pregnancy can be detected in more advanced pregnancy, and the incidence of hemorrhagic shock or peritonism is present in 1/3 of patients [202]. Live preterm fetuses can be delivered from hepatic pregnancy [207]. Most (93.5%) hepatic pregnancies involve the right lobe, mostly on its inferior surface [202]. Two mechanisms explain such a high incidence of this location of implantation: (1) peritoneal fluid circulation from the right paracolic gutter to the diaphragm due to intestinal and diaphragmatic movements and (2) effect of gravity—with the supine position, the lower surface of the right lobe of the liver is the lowest position of the abdominal cavity.

### 9.4.4 Clinical Presentation

Abdominal pain was the most common symptom, mainly in the right upper quadrant. Shoulder pain is rare, more commonly on the right side. Approximately 50% have amenorrhea or a history of vaginal bleeding with dark blood after menstruation [203]. Hemorrhagic shock or peritonism is present in 1/3 of patients. Gastrointestinal symptoms include vomiting, nausea, and abdominal distension, while gynecological symptoms are vaginal bleeding and discharge [202].

### 9.4.5 Differential Diagnosis

The leading symptom of upper right abdominal pain, primarily without (awareness of) amenorrhea, may mislead to digestive and hepatobiliary pathologies. Another misleading symptom is dyspepsia due to the close relation of the gallbladder and the duodenum [198].

### 9.4.6 Diagnosis

#### 9.4.6.1 Laboratory Findings

A complete blood count is mandatory for patients with abdominal pain and signs of hypovolemic/

hemorrhagic shock, including BUN, creatinine, liver, and pancreatic enzymes. Amenorrhea mandates  $\beta$ HCG testing. Without rupture and intra-peritoneal bleeding, complete blood count can be normal [203].

#### 9.4.6.2 Transvaginal Ultrasound

With elevated  $\beta$ HCG levels, transvaginal US defines the adnexa, the uterus, and gestational status. A normal-sized uterus with a thickened endometrium without an individual gestational sac is suspicious of EP.

#### 9.4.6.3 Transabdominal Ultrasound

Potential locations of EP should be checked, especially when Fallopian tube EP is excluded. Most hepatic gestations are subcapsular with an irregular mass that exceeds the contour of the liver, although some are located within the liver (Fig. 9.26). All confirmed cases included hemodynamically stable patients. Doppler can estimate the vascularity of the lesion (Fig. 9.27a).

#### 9.4.6.4 Abdominal CT

Contrast-enhanced abdominal CT is indicated when the transabdominal US is unequivocal in hemodynamically stable patients. While abdominal CT has been used in 32% of patients with an accuracy of 100% for splenic pregnancy [210], there are no data for hepatic pregnancy

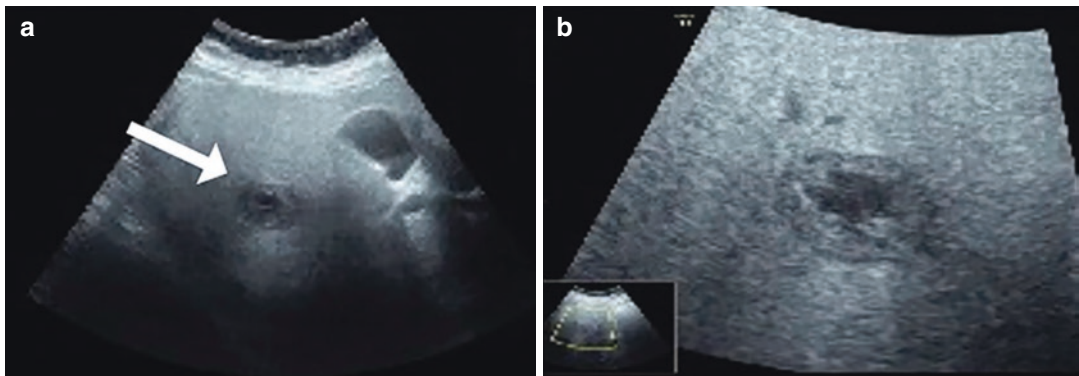
[202]. Except for the size and location of the gestational sac, the extent of the hemoperitoneum, primarily around the liver, can be defined (Fig. 15.27b–d). In more advanced pregnancy, fetal parts and placenta in the liver are visualized on CT [211] or MRI (Fig. 9.28).

#### 9.4.6.5 Abdominal MRI

For suspected pregnancy, MRI should be performed after the inconclusive US. It reveals the location and size of the gestational sac (Fig. 9.29). Noncontrast MRI, using T2-weighted imaging, is sensitive, specific, and accurate for hepatic EP. It usually showed a round-like, high-signal mass, mainly homogeneous, with unclear margins. At T1-weighted imaging, MRI displayed a hepatic round-like, low-signal mass with undefined margins. With contrast enhancement in the arterial phase, the hepatic pregnancy appears as a round-like, low-signal mass with no intensification in the central or peripheral portions. Noncontinuous ring-like intensification is displayed during the venous phase, with lower irregular intensification in the center [213].

#### 9.4.6.6 PET-CT

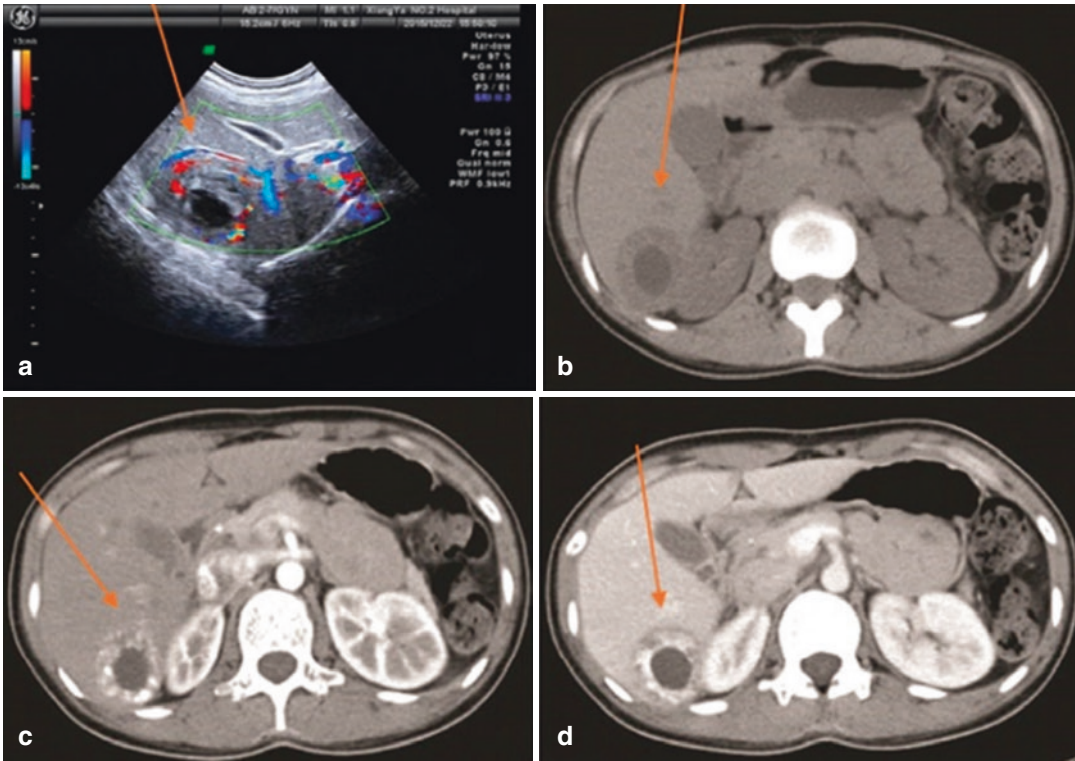
In one case report, PET-CT discovered unexpected hepatic pregnancy. The display indicated a lesion with glucose metabolism increased in the peripheral but not in the central portion (Fig. 9.30).



**Fig. 9.26** (a) Transabdominal US shows uneven fatty liver and a cystic echo mass (arrow) measuring  $30 \times 19 \times 25$  mm, (b) with a hypoechoic nucleus attached

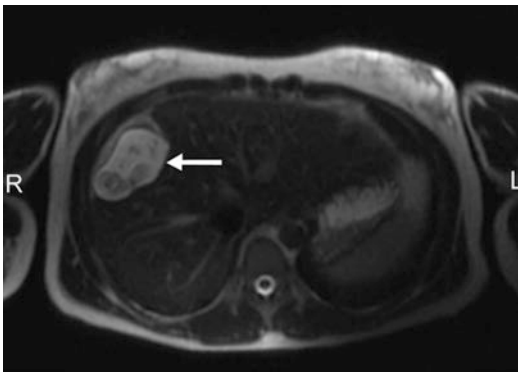
to the inferior surface of the right hepatic lobe. (Reproduced with permission from [208])





**Fig. 9.27** (a) Transabdominal US (no gestational sac in the uterine cavity) shows a  $5.4 \times 4.6$  cm hyperechoic mass (arrow) in the right hepatic lobe and a fluid sonolucent area of  $2.7 \times 2.1$  cm within the mass. The cystic sonolucent area within the fluid sonolucent area suggests an ectopic pregnancy. (b) CT reveals a mass in the right hepatic lobe (arrow) with a slightly low-density peripheral portion and an oval lower-density central portion in

the plain scan. (c) CT in the arterial phase shows a peripheral portion with a significantly increased density, a peripheral portion with a slightly increased density (arrow) compared with that of the liver parenchyma in the (d) venous phase shows a non-enhanced lower-density central portion in the enhanced scan (arrow). (Reproduced with permission from [209])



**Fig. 9.28** Abdominal MRI shows an intrahepatic lesion with fetal parts (arrow). A crescent-shaped area laterally represents placental tissue. (Reproduced with permission from [212])

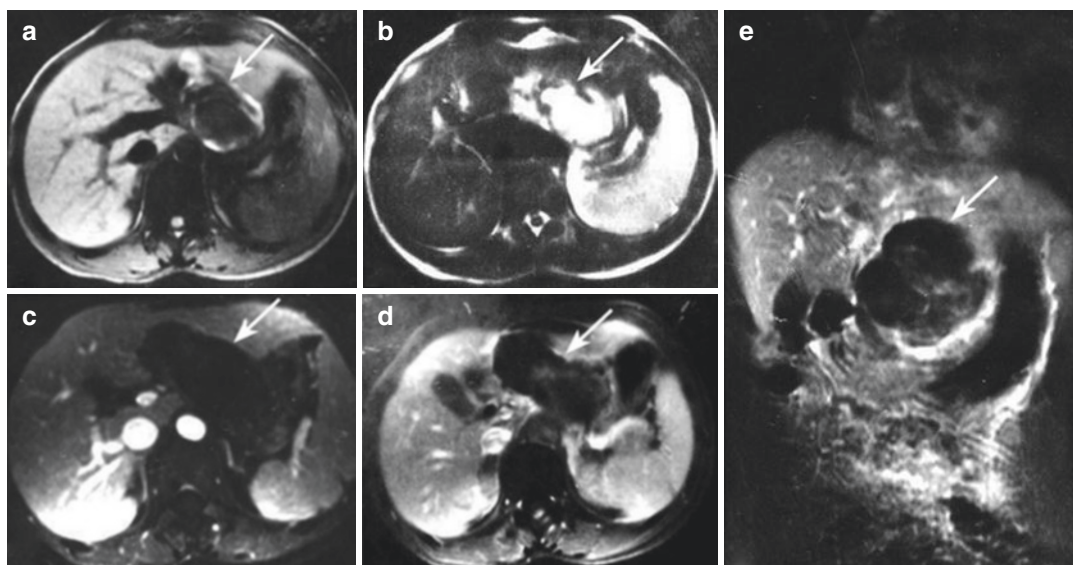
## 9.4.7 Treatment

Management primarily depends on the hemodynamic stability and location of the lesion.

### 9.4.7.1 Medical Treatment

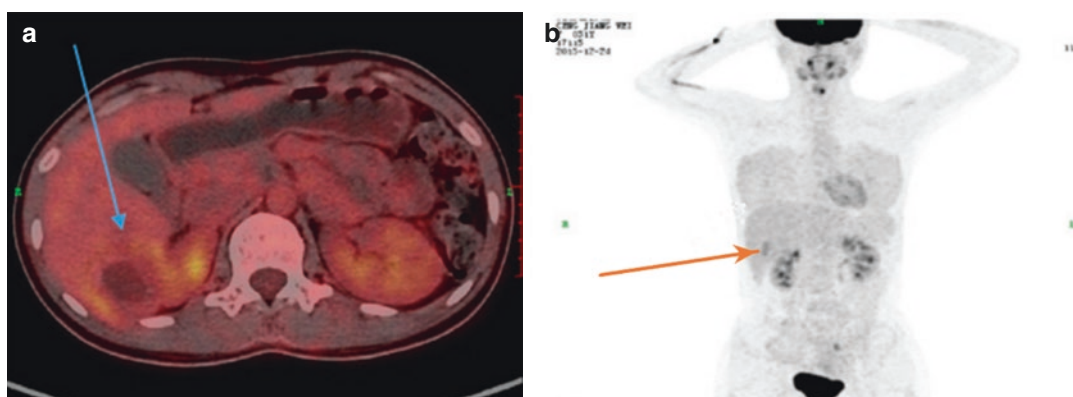
The gestational sac of  $>3.5$  cm is a relative contraindication for MTX treatment [212]. Medical treatment with IM MTX (1 mg/kg) can be administered when blood pressure, pulse, and body temperature are normal, in addition to a normal Fernandez score. Guarding or rebound tenderness should be absent. Laboratory findings should exclude acute bleeding; leukocyte count, platelet count, liver transaminases, and renal function





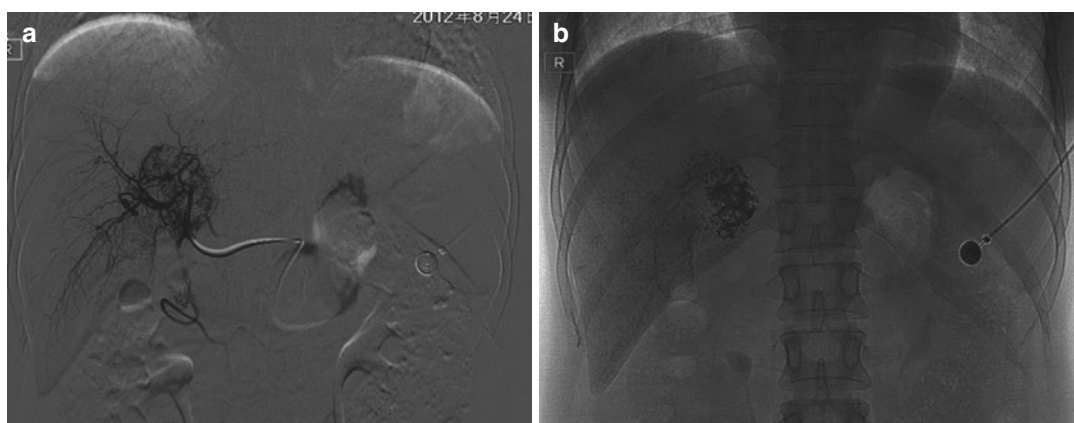
**Fig. 9.29** MRI characteristics of primary hepatic pregnancy. (a) T1 reveals a round low-signal focus ( $3 \times 4.5$  cm) between the inferior margin of the left hepatic lobe and the lesser curvature of the stomach. Most edges of the focus are clear. (b) T2 reveals the focus appears to be obvious high signals, most of which are homogeneous. (c) The focus appears to be low elliptical signals with enhanced MRI during the arterial phase, and there is no

sign of intensification inside the focus and on the edge. (d) Slight intensification is displayed in focus during the venous phase; a bit of ring-shaped intensification may be seen on the edge of the right frontal. (e) Coronal scan reveals that the disease takes on a round-like low signal with a slight noncontinuous ring-like intensification and slight irregular intensification inside [213]



**Fig. 9.30** Positron emission tomography-CT. (a) A maximum intensity PET-CT shows hepatic pregnancy (blue arrow) (the same patient from Fig. 9.27). (b) Orange

arrow points to the location of the hepatic pregnancy. (Reproduced with permission from [209])



**Fig. 9.31** Hepatic angiography of primary hepatic pregnancy. (a) before transcatheter arterial chemoembolization (TACE), hepatic angiography shows a hypervascular lesion of residual trophoblast tissue in the right hepatic

lobe and its supply branch from the right hepatic artery; (b) after TACE, Lipiodol on X-ray is densely deposited in the lesion. (Reproduced with permission from [215])

should be normal.  $\beta$ HCG should be checked once a week for several weeks [214].

#### 9.4.7.2 Radiological Intervention Techniques

With bleeding hepatic pregnancy, selective embolization can stop the bleeding and stop the pregnancy by ischemia (Fig. 9.31). Other methods include US-guided fetal intracardiac potassium chloride and MTX alone or combined, united with maternal IM injection of MTX [212, 216]. Selective embolization is also indicated when (1) hepatic nodule cannot be removed completely because of deep implantation into the hepatic parenchyma and hilum [215], primarily when a hepatobiliary surgeon is unavailable; and (2) postoperative  $\beta$ HCG is rising [215].

A common femoral artery approach is common. A mixture of 6 mL of Lipiodol (iodized oil; Guerbet, Roissy, France) and 50 mg (1 mg/kg) of MTX is infused via the microcatheter as close as possible to the feeding branch, followed by embolization of the feeding artery with gelatin sponge particles (0.5–1.0 mm). An MTX–Lipiodol emulsion is used to localize the MTX inside the hepatic lesion and release it

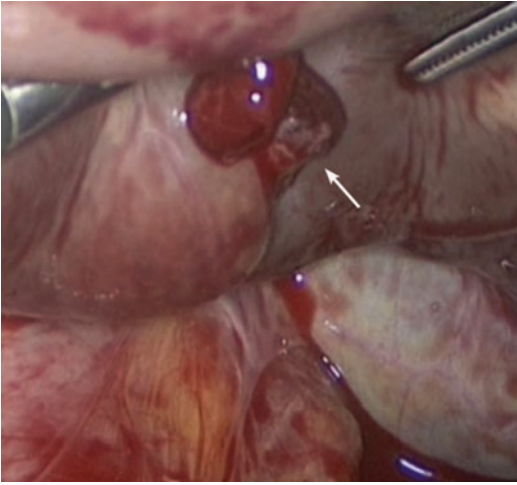
slowly. After embolization, an X-ray confirms the deposition of Lipiodol inside the lesion (Fig. 9.31b).

Another option is US-guided MTX or KCL intragestational sac injection transhepatically [212]. Both procedures eliminate surgical complications.

#### 9.4.7.3 Surgical Treatment

Significant bleeding or hemorrhagic shock should be treated with surgical hemostasis. Until 2018, 84% were treated by laparotomy [202]. Intraoperatively, clot-like bulging is found on the surface of the liver, with bleeding from that site (Fig. 9.32). Different surgical procedures are used, including omental transplantation, hepatic artery ligation, liver packing, lobectomy with fetus, and laparotomy combined with intraoperative intragestational injection of 20–25 mg. MTX (for gestational sac <35 mm) or potassium chloride, laparotomy with a maternal postoperative injection of MTX, and postoperative hepatic artery embolization [202, 217].

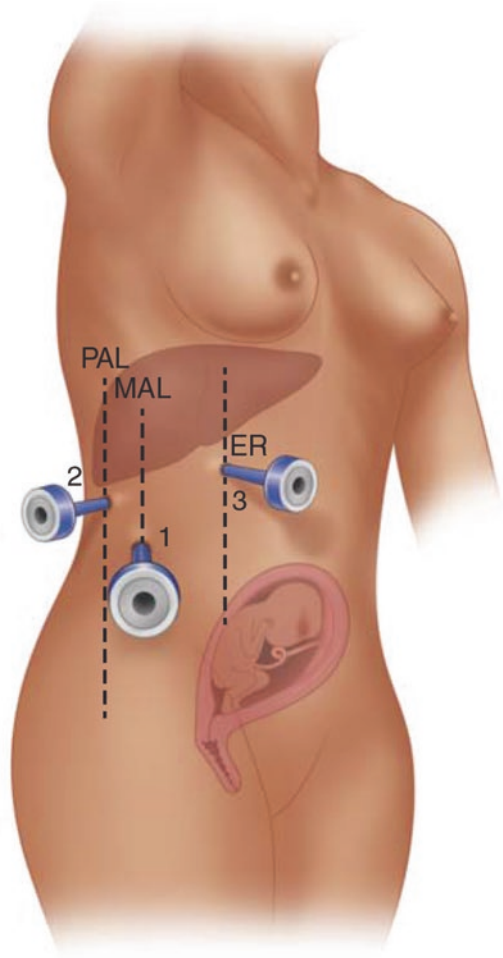
The intragestational sac injections producing fetal death by cardiac arrest eliminate the need to extirpate a gestational sac in the liver. This mini-



**Fig. 9.32** Bleeding from hepatic segment 6: a 3-cm bulging mass was detected. This area presented with a smooth surface covered by Glisson's capsule. Trophoblastic-like material and active bleeding emerged from a break in the continuity of 1 cm (arrow). (Reproduced with permission from [201])

mizes the possibility of hepatic bleeding or biliary tract injury. In more advanced pregnancies, maternal MTX involutes the placenta and fetal tissue and reduces the risk of bleeding. The timing of MTX administration related to surgical procedures is not defined. It can be administered preoperatively via IM injection, intraoperatively into the location of implantation, or postoperatively via IM injection. Postoperative IM administration is routine or selective if postoperative  $\beta$ HCG values rise [218].

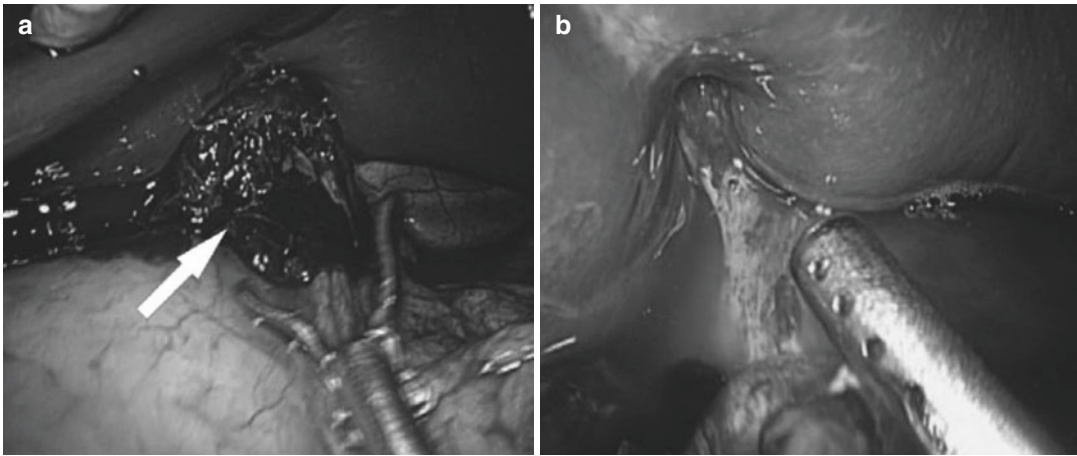
Laparoscopy is increasingly used for surgical hemostasis and EP removal in hemodynamically stable patients [201, 209, 218]. The trocar position depends on the location of the gestational sac in specific liver segments (Fig. 9.33). The suction of blood clots and EP is followed by hemostasis of the bleeding spot with topical hemostats (Fig. 9.34). Pathophysiology of evacuated contents confirms blood clots with clusters of cytotrophoblasts and syncytiotrophoblasts, consistent with EP. The pathohistological analysis of resected gestational sac reveals hepatic tissue and products of conception (Fig. 9.35).



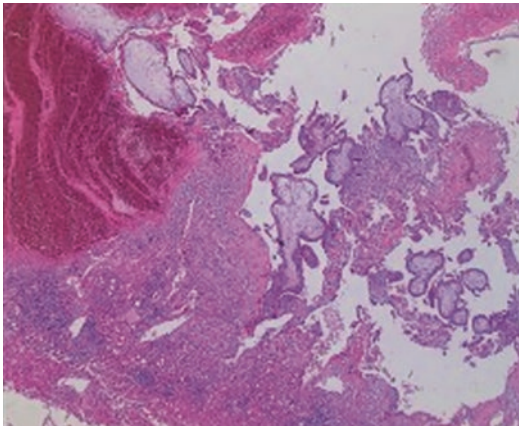
**Fig. 9.33** The liver segment 6 gestational sac location necessitates the left lateral decubitus position. The first trocar inserted by open technique is in the subcostal right region at the midaxillary line (1). Another two trocars are placed under direct visualization in the right flank (2) and the epigastric region (3). ER epigastric region, MAL midaxillary line, PAL posterior axillary line

#### 9.4.7.4 Continuation of Pregnancy and Delivery

Expectant management is possible in centers with immediate recourse to emergency interventions and neonatal care. The transabdominal US should detect a viable pregnancy with adequate amnion and an absence of congenital abnormalities. The oligohydramnios on US and abdominal pain warrant intervention [207].



**Fig. 9.34** Primary hepatic pregnancy (*arrow*) implanted on the liver hilum and removed (a) piecemeal and (b) with the aid of suction. (Reproduced with permission from [218])



**Fig. 9.35** Histologic examination of the resected specimen shows chorionic villi infiltrating into the liver tissue (H&E,  $\times 40$ ). (Reproduced with permission from [208])

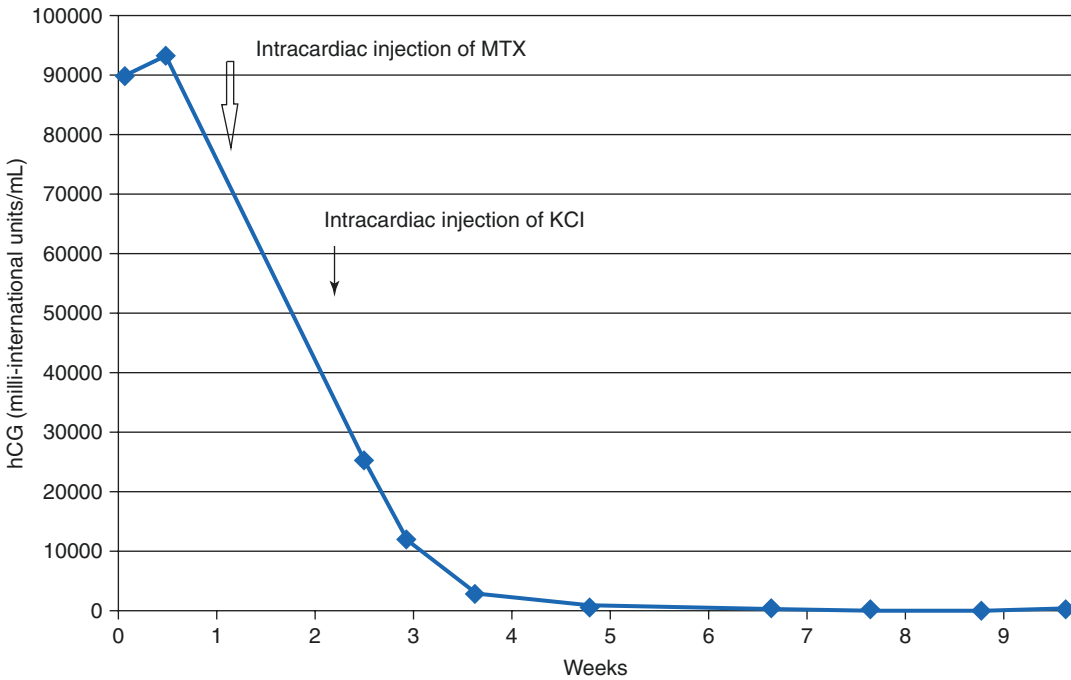
With fetal viability, operative delivery is indicated by median laparotomy or (extended) subcostal incision. Following the dissection of the surrounding organs (mostly bowel) off the placental membranes, the amniotic cavity is entered

through an avascular area to deliver a live newborn. No attempt is made to remove the placenta. Bleeding from the membrane edges is controlled by interlocking sutures and gauze packs. For inadequate bleeding control, gauze packs were removed after 48 h [207].

#### 9.4.7.5 Anesthetic and Perioperative Management

See Chap. 2. The operative specimen should be sent to the pathohistological examination, which reveals gestational villi in the hepatic mass. With retained placenta and gestational parts, serial serum  $\beta$ HCG and the transabdominal US during the first several weeks detect the continuation of hepatic pregnancy (Fig. 9.36). Maternal renal and liver function tests should be checked before and after MTX administration. With the remaining gestational sac, successful intrauterine injections result in the disappearance of  $\beta$ HCG levels within 4 weeks [212, 217].





**Fig. 9.36**  $\beta$ HCG trend after fetal intracardiac injection of MTX (unsuccessful) and KCl (successful) after a week. MTX methotrexate, KCl potassium chloride. (Reproduced with permission from [212])

## 9.5 Primary Ovarian Pregnancy

### 9.5.1 Historical Perspective

De Saint Maurice of Périgord (former province of France, which corresponds roughly to the current Dordogne) was the first to observe a case of ovarian pregnancy in 1682. It was a letter in a French journal composed by the Abbe de la Rocque. It was translated to the Latin, in the *Bibliothèque Anatomique de Manget, tome premier*, page 623. The fetus was lying in the abdominal cavity after being torn from the ovary, surrounded by blood. The laceration was visible on the ovary. The patient died of intraperitoneal hemorrhage, and the diagnosis was made post-mortem [219]. Without exacting laboratory examination, ovarian apoplexy [220] may often be misconstrued as an idiopathic event when early abortion of an ovarian pregnancy has occurred. Another misdiagnosis was bleeding corpus luteum [221].

### 9.5.2 Incidence

Paul Moulouguet-Doleris, in 1924, reported 77 cases [222], and CR Strother-Stewart, in 1953, reported at least 125 cases in the English literature [223]. The incidence of primary ovarian EP is increasing. In the 1950s, it was estimated from 1:25,000 to 1:40,000 [224]; in the 1980s from 1/5000 to 1/8000 [225] and even 1:2850 [226]. Of all ovarian pregnancies, 75–90% are primary [225, 227]. In the first half of the twentieth century, 75.5% were terminated during the first trimester, 12.2% during the second trimester, and 12.2% lasted to the third trimester or beyond [224]. HP with ovarian EP is exceedingly rare, comprising <2% of cases [227]. The incidence of ovarian EP is still likely underestimated due to the possibility that certain cases were successfully treated with MTX, but were denoted as tubal pregnancies or pregnancies of unknown location [24, 227, 228].



Both ovaries are equally affected [225, 227, 229], except in women with IUCDs, where the right side is almost exclusively affected [230–232], although left-sided cases exist [221].

### 9.5.3 Risk Factors and Pathophysiology

Risk factors for EP that include ovarian pregnancy [224, 225] are presented in Table 9.1. The most common are previous abdominal surgery, endometriosis, and IVF [233]. The IUCD is present in 4–68% of ovarian pregnancies [225, 227, 229, 234]. The association between ovarian pregnancy and IUCD use was recognized in 1930 [235]. The Lippes' loop's free end pointed towards the affected side in each case [236]. Most cases occurred with the Lippes Loop\* in place and a single one with a Dalkon Shield [230]. From 1966 to 1983, 27% of ovarian pregnancy cases were associated with the IUD in the USA and involved the Cu-7 IUD [237], while in others, copper-based IUCS was present in 88% [229]. It has been suggested that Cu-7 does not increase or decrease the risk of ovarian pregnancy relative to inert plastic IUCDs [237]. During the 1960s and 1970s, the ratio of ovarian pregnancies to EP in IUCD users ranged between 1:7 and 1:13 [226, 229, 238, 239]; its prevalence in the general population is smaller but still increasing—from 1:332 [232], over 1:150 to 1:200 [225, 234], over 1:117 [224] to 1:40–1:63 [227]. Approximately 25% do not have known risk factors for (ovarian) EP [227].

Prostaglandin-mediated hypercontractility of the tubes in IUCD users may impair the pickup of the ovum [221, 240]. An IUCD causes alterations in the level of prostaglandins in the different segments of the Fallopian tube with inverse peristalsis and reversed suction [236]. Changes in tissue levels and the ratio between the concentration of prostaglandin E and prostaglandin F are essential for tubal peristalsis [241]. Also, a significantly larger number of mast cells is present in the tubal

stroma of IUCD users than in controls [242]. Prostaglandins are mast cell mediators [23]. The mast cells are situated nearer to the smooth muscle cells in the tube than to the small vessels due to their role in tubal peristalsis [22]. Different types (including composition, hormones, and concentrations) of IUCDs could have different influences on ovarian pregnancy rates [229].

In 1876, Ferdinand Hueppe, in an inaugural dissertation, established the conditions to consider an ovarian pregnancy: (1) fecundation on the ovary, the ruptured follicle closing itself afterwards, and the fetus developing in the interior of the ovary as a cyst; (2) the ruptured follicle does not close itself, but the placenta retains its implantation in the ovary [243].

*Spiegelberg criteria* from 1878 differentiate an ovarian pregnancy from a tubal pregnancy [244]:

- gestational sac is in the region of the ovary,
- EP is attached to the uterus by the ovarian ligament,
- histologically proven ovarian tissue in the wall of the gestational sac,
- Fallopian tube of the involved side is intact.

Norris, in 1909, further amplified the first postulate by stating that the tube must show no microscopic evidence of pregnancy [245]. Stander enlarged the fourth postulate by requiring ovarian tissue to be found in several places at some distance from each other in the sac wall [246]. Further modification of Stander's modification is that ovarian tissue must be demonstrated in the sac walls in several places at some distance from each other and intervening between fetal tissues and any adherent extraneous tissue [224].

Baden and Heins suggested functional classification of "primary ovarian pregnancy" based on the implantation site and later development of the fertilized ovum. Ovarian tissue forms an intact layer around the embryonic tissues. It is subdi-

vided into *intrafollicular*, in which the fertilized ovum is implanted and develops in the Graafian follicle, and *extrafollicular*, in which the ovum is implanted and develops in the ovarian stroma. This type includes juxtafollicular, interstitial, cortical, and superficial implantation. In “combined ovarian pregnancy,” the ovary forms at least a portion of the tissue lying adjacent to fetal tissues but not forming the entire wall by itself. In addition, forming the rest of the sac wall and lying adjacent to fetal tissues would be other organs [221].

The cause of implantation anomalies in ovarian EP is not clear, resulting in various hypotheses [61]:

- delay of ovum liberation (ovum may be retained in the ruptured follicle, or the internal liquor pressure in the follicle may not be high to extrude the ovum),
- thickening of tunica albuginea (from oophoritis),
- tubal dysfunction,
- IUCD.

The corpus luteum is located almost exclusively in the same ovary as the pregnancy [223, 229, 232, 237, 247].

IUCD pregnancies have cases with ovarian pregnancy on one side and corpus luteum on the other [230].

Cases of ovarian EP progressing into the second or third trimesters remain exceptional [248–251]. The EP pregnancy usually ruptures in early gestation [51, 252].

## 9.5.4 Clinical Presentation

The signs and symptoms of ovarian pregnancy are usually indistinguishable from Fallopian tube EP [221] (see Sect. 9.1.4). The most common symptoms are abdominal pain (42.9%) and vaginal bleeding (28.6%). Up to 1983, 91.6% of

ovarian EP had ruptured before laparotomy [225]. Ruptured ovarian EP decreased in incidence since the increased use of transvaginal US and serial serum  $\beta$ HCG [253]. Almost 10% are asymptomatic with incidentally discovered ovarian pregnancy during post-IVF monitoring [227].

## 9.5.5 Diagnosis

### 9.5.5.1 Laboratory Findings

See Sect. 9.1.6.1.

### 9.5.5.2 Transvaginal Ultrasound

The transvaginal US shows a free fluid in the pouch of Douglas, with an appearance characteristic of organized clots depending on the severity of bleeding. There is no evidence of an intrauterine gestational sac. Vascular proliferation around the gestational sac called the ‘*ring of fire*’ is typical for ovarian pregnancy. The unruptured ovarian pregnancies have the characteristic solid hyperechoic rings or masses, and the correct preoperative diagnosis is approximately 50% [227]. No characteristic US was detected in the ruptured ovarian EP, and all were diagnosed as ruptured EP or corpus luteum by the preoperative US. A corpus luteum may have a ring-like appearance, but in most cases, a corpus luteum is less echogenic than the ovary [254].

### 9.5.5.3 Culdocentesis

Until 1983, culdocentesis was performed in 20.8% and was always positive [225]. Almost all ovarian pregnancies ruptured before exploration, which can cause 100% of positive culdocentesis. Today, it is rarely performed.

## 9.5.6 Differential Diagnosis

Due to the most frequent ovarian EP rupture in early gestation, the most common differential diagnoses are bleeding corpus luteum (cyst), Fallopian tube EP, (torsion) of an adnexal mass, or acute appendicitis [221, 227, 230].



**Fig. 9.37** (a) Intraoperative photograph of the normal uterus, the left round ligament, and the left Fallopian tube. The ovary contains the gestational sac. (b) An operative aspect of the left ovary after resection and ablation of the

gestational sac and hemostatic suture. (c) H&E stain shows decidual cells, trophoblastic elements, and the ovarian capsule. (Reproduced with permission from [261] under the CC BY 2.0)

## 9.5.7 Treatment

### 9.5.7.1 Medical Treatment

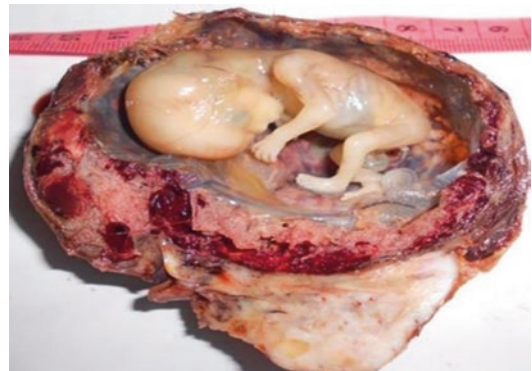
See Sect. 9.1.7.2. Medical and conservative treatments have been introduced recently to prevent ovarian tissue loss and pelvic adhesions and preserve the patient's fertility [255–257]. MTX treatment is chosen after a clear diagnosis and detection of the localization of EP by laparoscopy as a supporting diagnostic procedure [258]. In cases where the gestational sac is <30 mm, without fetal cardiac activity, and <6 gestational weeks, MTX treatment is preferred. It is superior to surgery because it does not disturb fertility [259]. Another option is an injection of etoposide [260].

### 9.5.7.2 Surgical Treatment

When maternal IM MTX treatment is ineffective, operative treatment is indicated.

Laparoscopy is increasingly used. Current reports show that 86% of laparoscopic access due to the adequacy of conservative surgery (ovarian wedge resection ± salpingectomy) is adequate for definitive treatment [227].

The state of the ovary dictates further treatment. If the remaining ovary looks normal, then wedge resection [221, 252], including the gestational sac, is indicated (Fig. 9.37). Hemostasis is completed with the bipolar current, followed by hemostatic sutures. Antimitotic drugs like MTX are added when the decrease of the level of  $\beta$ HCG is not sufficient [7]. When the ovary is much altered (Fig. 9.38), total oophorectomy



**Fig. 9.38** After adnexectomy of a mass, an ovary measuring  $9 \times 9 \times 5$  cm, with a gestational sac of 7 cm long axis, was found. A dead male fetus was within the sac. (Reproduced with permission from [262] under the CC Attribution License)

[221] or adnexectomy is indicated. The specimen is retrieved using an endobag to eliminate the possibility of secondary implantation [252]. Careful examination of the blood and clots from the hemoperitoneum associated with bleeding from the ovaries is necessary to establish the diagnosis of ovarian EP since all the products of the ovarian EP may be flushed into the peritoneal cavity [240, 263]. Placental tissue in specimens removed from bleeding corpora lutea confirms ovarian EP [221, 252]. In 1983, 50% were treated by ovarian cystectomy or wedge resection [225].

Follow-up should include serial serum  $\beta$ HCG measurements until the levels become undetectable [252].

## 9.5.8 Prognosis

### 9.5.8.1 Maternal Outcome

Maternal mortality, starting from 1952 to 1980, was 0% [225]. The future fertility in patients with an ovarian EP is good since the early rupture of the ovary requires conservative surgical management, and tubal function is commonly unaffected [229]. Among women who wanted to conceive after ovarian pregnancy, a tendency to better fertility among IUCD users than non-IUCD users was found [229].

### 9.5.8.2 Fetal Outcome

In the first half of the twentieth century, of the viable ovarian gestations (12.2% of all cohort), 63.3% were stillborn and 36.4% were alive at birth. Half of the alive at birth were grossly malformed [224].

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# Uterine Rupture and Perforation

# 10

## Abstract

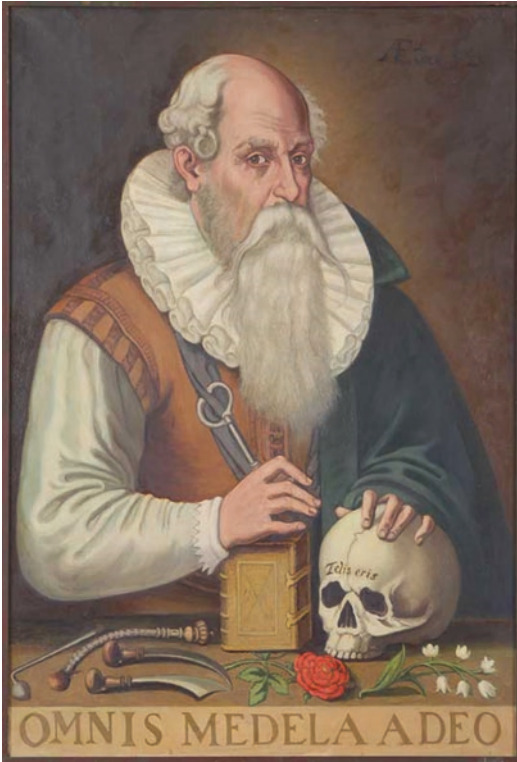
Nontraumatic uterine rupture is a rare but often catastrophic obstetric complication with an overall incidence of approximately 1/1536 pregnancies. In western countries, it is five times less common. Most spontaneous uterine ruptures occur in women with uterine scars, mostly due to previous Cesarean deliveries. The most consistent early indicator is prolonged, persistent, and profound fetal bradycardia. Abdominal pain, abnormal progress in labor, and vaginal bleeding are less consistent and less valuable in establishing the appropriate diagnosis. Cesarean delivery should start within 20–30 min of fetal distress. Fetal or placental extrusion through the uterine wall mostly results in irreversible fetal damage. Therefore, such a recommendation is of limited value in preventing major fetal and neonatal complications. However, immediate supportive and resuscitation methods within this period prevent maternal exsanguination and death. This is followed by definitive surgical intervention. Traumatic uterine rupture mostly results from maternal blunt abdominal trauma. Pathophysiology is similar to nontraumatic rupture. Uterine perforation is rare. It results from maternal stab or gunshot wounds.

Ruptures occur during the increased pressure on the organ, either from outside or inside. Ruptures can be spontaneous or traumatic. Perforation occurs when the underlying pathologic process destroys or penetrates the organ wall.

## 10.1 Spontaneous Uterine Rupture

### 10.1.1 Historical Perspective

One of the first descriptions of spontaneous uterine rupture (UR) was by Wilhelm Fabry (also William Fabry, Guilelmus Fabricius Hildanus, or Fabricius von Hilden) in the seventeenth century (Fig. 10.1). The first case was a multigravida during labor at term with the UR due to fetal transverse lie. The second was a fatal case of UR caused by obstructed labor [2]. In James Dowling Trask's (1821–1883, one of the founders of the *American Gynecologic Society*) monograph on UR, 303 cases were recorded from 1700 to 1848; only 38 were classified as URs during pregnancy, the others being cases of UR during labor. Real numbers are smaller when cases are excluded that are some other condition or premature labor. When this reduction has been made, 14 cases remain [3]. Cooper, in 1858, described the post-mortem findings of UR, in the third month of



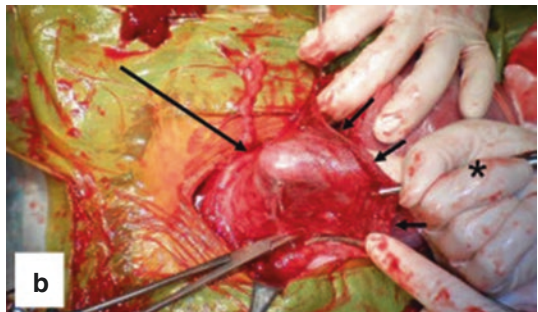
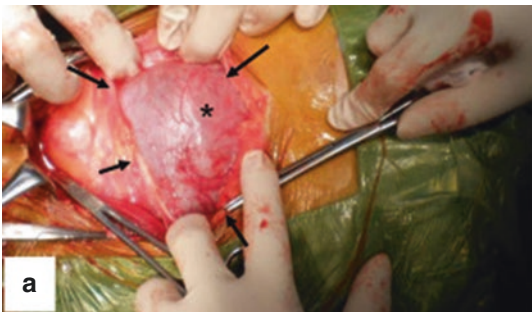
**Fig. 10.1** Wilhelm Fabry (June 25, 1560–February 15, 1634), often called the “Father of German surgery,” was the first educated German scientific surgeon. He is the author of 20 medical books. His *Observationum et Curationum Chirurgicarum Centuriae*, published posthumously in 1641, is the best collection of case records of the century. (Reproduced with permission from [1] under the CC Attribution License)

pregnancy, from tuberculous degeneration of the fundus [4]. A further collection of 98 UR cases was by R. P. M. Ames (the Philadelphia Hospital and the Jefferson Medical College Hospital, Philadelphia) in 1881 [5] and A. Lewers (17 cases) in 1887 [6]. In 1903, Baisch recorded 37 nontraumatic URs in the first 6 months of pregnancy [7].

### 10.1.2 Definition and Classification

UR is a disruption of the uterine muscle and visceral peritoneum or a uterine muscle separation extending to the bladder or broad ligament. UR can be incomplete or complete.

**Incomplete (partial) uterine rupture** is present when the uterine wall is extremely thinned, and the uterine muscular layer is lost, but the uterine serosa (parietal peritoneum) is preserved (Fig. 10.2). One example is the laceration that opens from the uterus into the broad ligament but with the anterior and posterior leaves of this structure remaining untorn. Incomplete UR is common with scar dehiscence. In contrast to a frank UR, *uterine scar dehiscence* disrupts and separates a preexisting uterine scar after CS. Uterine scar dehiscence is a more common event than UR. Importantly, the defect in the uterine wall limited to scar dehiscence does not disrupt the overlying visceral peritoneum. It does



**Fig. 10.2** Operative findings at a Cesarean section. (a) The thin anterior uterine wall (asterisk) with a bulge caused by fetal parts from the inside. Arrows indicate the peritoneum. The left side of the photograph is the caudal side of the patient. (b) After delivery and removal of the

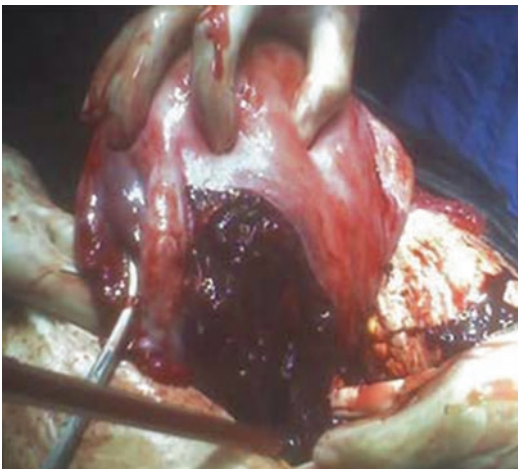
placenta, the thin wall is gently pushed from inside the uterus with a finger. The fingertip (large arrow) is visible through the thin wall. The asterisk indicates the surgeon's right hand. Small arrows indicate the uterine incision site. (Reproduced with permission from [8] under the CC BY 2.0)

not result in clinically significant bleeding from the edges of the preexisting uterine scar. In addition, in cases of uterine dehiscence (as opposed to UR), the fetus, placenta, and umbilical cord remain contained within the uterine cavity.

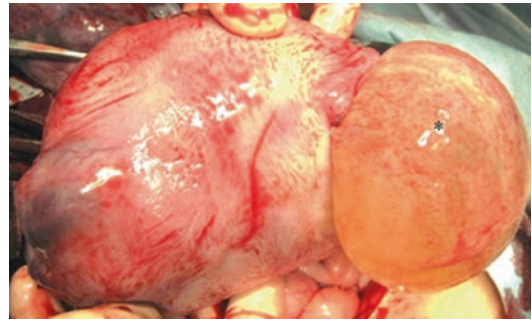
**Complete uterine rupture** is present when rupture occurs through all layers of the uterine wall, including serosa with or without accompanying bleeding or hematoma (Fig. 10.3). Therefore, the amniotic cavity directly communicates with the abdominal cavity. Approximately 70% have a complete UR and 25% have an incomplete UR. Seventy percent of scar ruptures presented with complete UR [10].

Additional factors dictate treatment strategy and prognosis: (1) placental abruption, (2) the expulsion of the fetus into the abdominal cavity, or (3) the expulsion of the amniotic sac (Fig. 10.4).

Several classification systems are related to UR etiology. The main classification is traumatic UR, spontaneous UR [12], or a combination of these. *True* spontaneous UR is a partial or full-thickness separation of the uterine wall before the onset of myometrial contractions that occurs primarily in the third trimester when the intrauterine volume and pressures are at the highest levels. Unfortunately,



**Fig. 10.3** Complete uterine rupture with a large left broad ligament hematoma with multiple minor bleeding points from the branches of the uterine artery. (Reproduced with permission from [9] under the CC BY 3.0)



**Fig. 10.4** Intraoperative appearance of the uterine fundus before placenta removal. Uterine rupture is at the right cornual area with prolapsed amniotic sac (\*). (Reproduced with permission from [11] under the CC Attribution License)

many cases were published under the term spontaneous but are not true spontaneous URs.

Schrinsky and Benson made an etiology-based classification in 1978 [13], which was further updated and expanded (Table 10.1).

Rickards, in 1938, described five types of UR of the scarred uterus during pregnancy [17].

**Type I** the rupture occurs through an old upper segment incision, and the placenta is situated away from the uterine scar. Characteristics include the following:

- The rupture tends to take place during labor,
- Little or no bleeding with a normal pulse,
- The pain may become niggling in type after the scar has started to give way,
- The bulging bag of membranes may sometimes be palpated through the abdominal wall,
- Prognosis is good, provided that suitable treatment is available.

**Type II** The rupture occurs through an upper segment incision, and the placenta is underneath the old scar. This type is more severe. When the placenta is underneath the old scar, the placental villi gradually erode fibrous tissue [18]. This erosion is insidious and may cause marked attenuation of the scar during the latter part of pregnancy. The rupture is more liable to occur before the onset of labor. The eating away of the scar may be associated with vague pains in the lower abdomen [19]. As the process is gradual, hemorrhage



**Table 10.1** Classification of causes of uterine rupture during pregnancy [13–16]

|                                                                                  |
|----------------------------------------------------------------------------------|
| <b>1. Traumatic rupture</b>                                                      |
| (a) <i>Instrumental</i>                                                          |
| Uterine sound or curette                                                         |
| Manual removal of placenta                                                       |
| Various tools for legal or criminal abortion                                     |
| (b) <i>Violence: direct or indirect</i>                                          |
| (c) <i>Obstetric</i>                                                             |
| Oxytocins, forceps, breech extraction                                            |
| Intrauterine manipulation: internal version, forceps rotation, shoulder dystocia |
| Fundal pressure                                                                  |
| Hydrocephalus                                                                    |
| Neglect: cephalopelvic disproportion, transverse lie                             |
| <b>2. Spontaneous rupture</b>                                                    |
| (a) <i>Previous uterine surgery</i>                                              |
| Cesarean section (scarred uterus)                                                |
| Myomectomy                                                                       |
| Salpingectomy                                                                    |
| Ventrofixation                                                                   |
| Curettage or manual removal of the placenta                                      |
| (b) <i>No previous surgery</i>                                                   |
| Congenital uterine abnormality                                                   |
| Cornual pregnancy                                                                |
| Hydatidiform mole or chorioadenoma destruens                                     |
| Placenta percreta                                                                |
| Genetic susceptibility for rupture (Loeys–Dietz syndrome)                        |
| Red degeneration of fibroid                                                      |
| Chronic corticosteroid use                                                       |
| IVF?                                                                             |
| No apparent cause                                                                |
| <b>3. Combinations</b>                                                           |
| Orgasmic uterine contractions                                                    |

is seldom severe. Characteristics include the following:

- Gradual rupture tends to occur toward the end of pregnancy. This may be accompanied by vague pain in the lower abdomen,
- After the onset of labor, bleeding may be of considerable severity,
- Prognosis will not be as favorable as type I and will depend mainly on the amount of intra-abdominal bleeding.

**Type III** The rupture occurs after a previous lower segment CS. Characteristics include the following:

- Rupture takes place during labor,
- Hemorrhage may occur due to the extension of the laceration laterally into the uterine arteries,
- The bladder may be involved, giving rise to hematuria.

**Type IV** The rupture is complete through an upper segment incision, and the child, within its bag of membranes, is expelled into the abdominal cavity, the placenta remaining in situ. The uterine scar separates, the contractions persist, and the child is extruded into the abdominal cavity. The fetal heart sounds almost invariably disappear, and fetal movements cease. The uterus is pushed over to one side, and the child, floating in the abdominal cavity, is palpable. Characteristics include the following:

- Fetal heart sounds cease as a rule,
- Fetal movements usually stop,
- The uterus is pushed to one side,
- The fetus, lying free in the abdominal cavity, is easily palpable.

**Type V** The rupture is complete through an upper segment incision, and the child, with its placenta, is extruded completely into the abdominal cavity. Characteristics include the following:

- Often associated with severe intra-abdominal hemorrhage,
- Fetal heart sounds are absent,
- Fetal movements are absent,
- The uterus is pushed over to one side,
- The fetus, lying free in the abdominal cavity, is easily palpable.

### 10.1.3 Mechanisms

#### 10.1.3.1 Scarred Uterus

##### Uterine Scar Rupture

Patients with uterine scars are more likely to have uterine scar rupture due to the attempted trial of labor and inadequate labor monitoring [20]. Most uterine dehiscences and ruptures in scarred uteri will occur via the uterine scar. The atrophic, inelas-

tic nature of the scar renders it less adaptive to forces in labor, predisposing it to rupture. Prostaglandins induce local biochemical modifications that weaken the scar, predisposing it to rupture [21]. In the trial of labor, secondary inertia may indicate that a partial or complete UR has interfered with the mechanism of labor. The blocking of the neuromuscular impulses is caused by the break in the continuity of the muscle [22]. In women with scarred uteri, catastrophic complete prelabor UR occurred mainly in scars outside the lower segment [23].

### Atypical Site Rupture

A particularly rigid anterior lower segment may cause the abnormal distribution of force. The posterior wall may be excessively shortened and thinned during retraction due to the rigid anterior uterine scar, catalyzing atypical UR via healthy tissue. Any factor compromising uterine structural integrity or causing abnormal force distribution can precipitate UR. The site of UR is unpredictable and may be atypical.

The lower segment UR is the most common (60%) site of rupture [24–27], with the anterior transverse location being the most common [28]. The second most common location is an extension to the broad ligament, and other locations have an incidence of around 5% [28]. Mostly there is no differentiation between UR caused by obstructed labor and scarred uterus. UR is complete in around 73% of cases and incomplete in 27% [24, 25, 27].

Posterior (posterolateral) UR complicating vaginal birth after low-transverse CS is rare [29–33]. Fetal malposition with an occipitoposterior position contributes to posterior UR (Fig. 10.5), as does malpresentation with a transverse lie [32, 33]. Malposition alters the distribution of contractile force and increases labor dystocia; certain malpresentations cause uterine hyperdistension, which may precipitate atypical UR. Prostaglandins generate excessive uterine activity increasing the UR rate. Prostaglandins may cause excessive uterine activity, resulting in a posterior wall sacculation of a strong anterior scar [31]. During the second stage of labor, with the fetus undergoing cardinal movements, UR occurs through the weakened posterior wall. In 50%, prostaglandins induced labor, suggesting



**Fig. 10.5** Vertical posterior rupture of the scarred uterus due to the occipitoposterior position of the fetus. (Reproduced with permission from [32])

other factors may play a role [33]. An inelastic scar comprising fibrous tissue on the anterior wall prevents the even distribution of contraction forces. As uterine muscle retracts during the active phase of labor, the healthy posterior wall may undergo excessive shortening and thinning compared to an inelastic anterior wall, which could predispose to rupture.

### 10.1.3.2 Unscarred Uterus

Obstruction as a cause of UR and the delay in accessing qualified care is found in developing counties with patients without antenatal care. The causes of UR during labor result from obstruction of vaginal delivery, whether the obstruction is a pelvic contraction, unusual size of the child, or malpresentation. The uterus continues to contract, with thickening of the upper part, while its lower segment becomes thinned. Without assistance, the lower segment becomes increasingly thinned and finally ruptures.

The rupture of the unscarred uterus during labor almost always begins in the lower segment.

A uterus emptied of its contents by their extrusion into the peritoneal cavity may retract firmly, preventing bleeding from the placental site and the wound in the uterus. The fetus and placenta do not necessarily escape at once or at all. It is the most common cause of spontaneous UR, ranging from 68.5% to 73.2% [20, 34] in developing countries. In developed countries, it is significantly lower, starting from 13% [35].

### 10.1.3.3 Simultaneous Uterus and Bladder Rupture

Simultaneous spontaneous UR and bladder rupture are common due to the same mechanism and location of obstruction and distension (see Sect. 28.3). It is more common with ruptures of unscarred uteri, which extend beyond the cervix [36].

## 10.1.4 Incidence

### 10.1.4.1 Developed vs. Undeveloped Countries

The rate of spontaneous UR during the last 50 years in developed countries has been increasing [37]. Table 10.2 shows the differences in incidence between countries. Preterm UR in the unscarred uterus is extremely rare in developed countries but is rising (1/333.333) [23]. In the developed countries, in the scarred uterus, there is a similar incidence of complete ruptures (1/5556), partial ruptures (dehiscences) at elective CS (1/5556), and partial ruptures at emergency prelabor CS (1/5263) [23].

Several issues arise with obtaining a true incidence. First, especially in Africa, registration of births occurring at home is incomplete, although the number of patients who deliver at home and only seek medical attention when problems occur decreases. Second, some maternal deaths occur in rural areas before hospital admission without known and registered causes of death. There are also significant differences between regions in the same country. The incidence of 1/167–1/200 deliveries was found in Southwest Nigeria [42, 43, 72], while in Northwest Nigeria was more than double (1/77 deliveries) [46, 47]. Third, because the health reforms policy of the govern-

**Table 10.2** (Spontaneous) uterine rupture rates across the world (in decreasing incidence)

| Country                   | Incidence       |
|---------------------------|-----------------|
| Ethiopia [34, 38]         | 1/38–1/175      |
| Uganda [20, 39]           | 1/93–1/200      |
| Pakistan [40]             | 1/100           |
| Yemen [41]                | 1/159           |
| Nigeria                   |                 |
| Southwest [28, 42–44]     | 1/186–1/416     |
| Rural [45]                | 1/112           |
| Northwest [46, 47]        | 1/77            |
| Guinea [48]               | 1/199           |
| Morocco [49]              | 1/222           |
| Sudan [50]                | 1/246           |
| India [51, 52]            | 1/357–1/714     |
| Kenya [53]                | 1/425           |
| Libya [54]                | 1/585           |
| Iraq (Basra) [55]         | 1/801           |
| Turkey [56]               | 1/966           |
| Saudi Arabia [57]         | 1/1011          |
| Nepal [10]                | 1/1100          |
| Australia [58]            | 1/1163          |
| Zimbabwe [59]             | 1/1285          |
| Rep. of South Africa [60] | 1/1362          |
| Trinidad [61]             | 1/1500          |
| Netherlands [62]          | 1/1695          |
| Bahrain [63]              | 1/2213          |
| Tunis [14]                | 1/2581          |
| Kuwait [64, 65]           | 1/1851–1/3333   |
| Israel [66]               | 1/2802          |
| Canada [67]               | 1/3333          |
| Taiwan [68]               | 1/3871          |
| Ireland [69]              | 1/4348          |
| Qatar [70]                | 1/4968–1/6843   |
| Singapore [71]            | 1/6331          |
| United States [12]        | 1/8000–1/15,000 |
| Norway [36]               | 1/10,000        |

ment in many countries prohibits refusal of admission of any medical emergency in all the state-owned public hospitals, larger hospitals receive many labor complications that occur in the primary and secondary health facilities and private hospitals. Therefore, the accurate incidence distribution among hospitals is not known. Fourth, some studies report cumulatively spontaneous (scarred and unscarred uterus) and sometimes traumatic URs [43]. Reports from Nigeria, Ghana, Ethiopia, and Bangladesh indicated that about 75% of UR cases were associated with the unscarred uterus [73], while in Norway, UR associated with the unscarred uterus is 33% [36].

For developed countries, the available data indicate that the prevalence of UR for women with previous CS is 1%, whereas it is extremely rare for women without previous CS ( $<1/10,000$ ). Overall, the rates are below 1/1000 [74].

10.1.4.2 Decade Dependency

The incidence is decade-dependent. The incidence of UR in the US between 1967 and 1978 was 1/1000–1/1500 deliveries, but spontaneous UR accounted for 25%, and only 17% of these occurred before the onset of labor [15]. After two decades, spontaneous rupture of the unscarred uterus ranged from 1/8000 to 1/15,000 deliveries [12, 75]. Due to the rarity of spontaneous UR, most studies have a study interval of around a decade to collect enough patients for analysis and comparison. With the progress of medicine and knowledge of the risk factors, the incidence is decreasing, but there are still significant differences between developed and undeveloped/developing countries (Fig. 10.6).

10.1.5 Risk Factors

Most spontaneous UR in undeveloped/developing countries is due to rupture of the unscarred uterus secondary to neglected obstructed labor. In

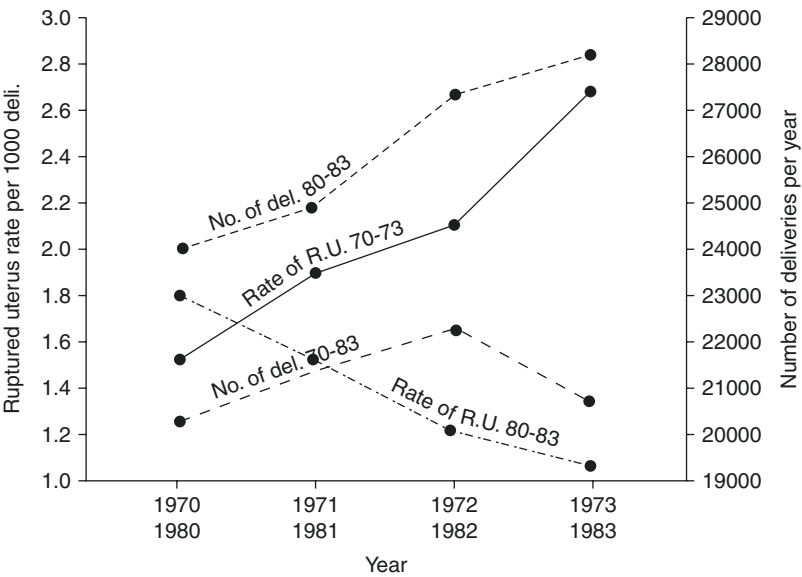
contrast, CS scar/scarred uterus is the most common cause in developed countries [72]. In developed countries, the rupture of the unscarred uterus is several fold lower than that of scarred uterus involving 1/17,000–1/20,000 deliveries [24].

Some recommend a continuous infusion of tocolytics to prevent UR with risk factors present [77].

10.1.5.1 Scarred Uterus

Eardley Holland, in 1920, made the first overview and found that 4% of Cesarean scars give way during a subsequent pregnancy or labor [78]. Previous CS is the most important predisposing factor for the occurrence of UR [79], and the so-called *scarred uterus* (uterine scars from any type of CS) is present in up to 65% of cases [57, 80]. It is conventionally attributed to the structural compromise of the uterine scar, as depicted by the term “trial of the scar.” The rate of CS has risen from 5% in 1970 to 26% in 2002 despite improvement in nonoperative obstetric procedures [81]. Relevant to vaginal birth after CS (VBAC) in the USA is its increasing rate, from 3.4% in 1980 to 28% in 1996. With an eightfold increase in the VBAC rate, maternal and perinatal morbidity also increased, particularly UR. By 2007, the VBAC rate in the USA had fallen to 8.5%. The CS rate

**Fig. 10.6** Comparison of the total number of deliveries in 1970–1973 and 1980–1983 with the rate of ruptured uterus per 1000 deliveries in those years in South Africa. The numbers for 1983 are a multiplication of the first 6 months. R.U. rupture of the uterus. (Reproduced with permission from [76])



also reached an all-time high of 32% in 2007. In its recent guidelines on VBAC, the *American Congress of Obstetricians and Gynecologists* (ACOG) adopted the recommendation not to restrict women's access to VBAC [82]. This occurred after the *National Institutes of Health Consensus Development Conference Panel* reviewed the totality of the evidence concerning maternal and neonatal outcomes relating to VBAC [83]. UR affects 0.7–1.9% of women with previous CS attempting a trial of labor [84]. The reported recurrence rate for UR is 4.8–19%, with the highest rates seen in women with a history of a ruptured upper uterine segment (classic scar). In these cases, planned CS is recommended [85].

### Classic Cesarean Delivery

Classic CS via vertical midline uterine incision is currently infrequently performed and accounts for 0.5% of all births in the USA [86]. There is an 11.5% absolute risk of UR in women with classic vertical CS scars who underwent an unplanned trial of labor after CS (TOLAC) [87]. The UR rate for women with prior classical uterine CS scars was 0.64% for women who underwent repeat CS. All patients underwent repeat CS, but a high rate of preterm labor resulted in 49% being in labor during CS [86]. An absolute UR rate in women with a previous classic, inverted T, or J incision presented in advanced labor or refused repeat CS was 1.9% [88]. These rates of frank UR in women with classic CS contrast with the higher rates of 4–9% that the ACOG had historically reported for women with these types of uterine scars [89]. However, there is a 9% rate of asymptomatic uterine scar dehiscence [86]. This suggests that disruptions of uterine scars might have been misclassified as true UR instead of dehiscences.

### Low-Vertical Cesarean Section

There is a 1.1% absolute risk of symptomatic UR in women undergoing a TOLAC with a low-vertical CS scar [88, 90]. Compared to women with low-transverse CS, there is no significantly increased risk of UR or adverse maternal and perinatal outcomes. Inconsistencies hamper the interpretation of how high the lower uterine segment could be cut before it was considered a clas-

sic incision. Even when the lower uterine segment is already well developed due to active labor, a low-vertical incision of adequate length is often impossible to permit fetal delivery. *The classic extension* is arbitrarily defined as a 2 cm extension into the upper segment, and the overall rate of UR was 0.62%. This rate could be further divided as 1.15% for women who underwent a TOLAC compared with no UR among women who underwent elective repeat CS [90].

### Unknown Uterine Scar

In many instances, the type of incision used for a prior CS cannot be confirmed due to the unavailability of the operative report. Under these circumstances, the assessment of UR risk may sometimes be guided by the obstetric history to infer the most probable type of uterine scar. For example, a patient with a history of a preterm CS at 28 weeks' gestation has a much higher likelihood of having had a vertical uterine incision than a patient who underwent a CS to indicate the arrest of fetal descent at term. Probably because most CS in the USA is accomplished via low-transverse uterine incisions, the risk of UR with an unknown scar and previous low-transverse hysterotomy is similar. This logic depends on the high ratio of low-transverse to vertical incisions performed for CS. However, it ignores the varying probability that different types of uterine incisions are made under different obstetric circumstances and differences due to varying medical resources and the prevailing local practitioner practices in countries other than the USA. An estimated 20,000 African refugees enter the USA each year, 80% from countries where the upper uterine segment CS is not an uncommon practice. The immigration of African refugees to Europe is becoming increasingly common. Nevertheless, most CS performed in the USA is accomplished via low-transverse uterine incisions.

Underpowered small case-control studies did not find an association between an unknown uterine scar and UR risk [91, 92]. The *Maternal-Fetal Medicine Units Network Cesarean Delivery Registry* reports a 0.5% risk of UR for patients who underwent a TOLAC with an unknown uterine scar [88]. A small, randomized, controlled trial



compared labor augmentation with oxytocin with no intervention in women with prior CS involving either one or two unknown uterine incisions. All uterine dehiscences and UR occurred in the group that underwent labor augmentation [93].

### Low-Transverse Cesarean Section

The myometrium from the scarred low uterine segment has a higher collagen content than the unscarred myometrium from laboring women but not unscarred myometrium from nonlaboring women [94]. The UR risk after a low-transverse CS varies depending on whether patients undergo a TOLAC or an elective repeat CS, whether labor is induced or spontaneous, and other factors. Today, the vast majority of CS is of the low-transverse type. Examining the various risk factors for UR is instructive for women with one previous CS. CS has potential complications, including an increased risk of placenta previa and accreta with every subsequent repeat CS, resulting in higher rates of peripartum hysterectomy [95]. The trend of an increasing rate of UR with increasing maternal age was noted [96, 97]. Age-related decreases in myometrial strength [98] and defective wound healing [99] could contribute.

### Cesarean Section Without a Subsequent Trial of Labor

The spontaneous UR rate among women with a single CS scar who underwent scheduled repeat CS without a TOLAC is 0.16% [100]. The uteri with CS scars have an intrinsic propensity for the UR that exceeds that of the unscarred organ during pregnancy, which is 0.012% (OR 12). Therefore, all other UR rates in women with a previous CS should be referenced to this expected baseline rate.

### Cesarean Section with Subsequent Spontaneous Labor

The UR rate among women with a single previous CS who labored spontaneously during a subsequent singleton pregnancy is 0.45–0.72% [100, 101]. This rate of UR implies an increased relative risk of 3–4 for women who labor spontaneously compared with women who undergo elective repeat CS.

### Cesarean Section with Subsequent Augmentation of Labor

There is a wide variance in the frequency of clinical use of oxytocin and the dose and dosing schedules. As a result, there is a paucity of specific evidence-based clinical guidelines for using oxytocin in VBAC trials. UR rate in women who underwent oxytocin augmentation of labor after a previous CS was 0.9–1.4%, compared with 0.34–0.4% in women who underwent a trial of spontaneous labor (two-fold to fourfold increased risk) [83, 102]. Others claim that labor augmentation with oxytocin does not increase the risk for UR in the scarred or unscarred uterus [101, 103]. However, the conclusions to be drawn from this are both limited. Therefore, the duration of labor and not oxytocin use itself may predispose the patient with or without a uterine scar to rupture. The problem in some studies from developing countries is the high percentage of its use; 41.7% of the respondents were given this drug (all but one had it through IV infusion) [41]. Oxytocin was used to augment prolonged and obstructed labor rather than for active labor management, concluding that supervision and control over this drug are missing. In this regard, assessing the safety of oxytocin use in VBAC trials must consider both the dosage and exposure time. At an intravenous oxytocin dosage range of 6–20 mU/min, a more than threefold increased risk of UR was associated with oxytocin use. At a dosage range of more than 20 mU/min, a nearly fourfold increased risk of UR was noted. The attributable risk associated with oxytocin use was 2.9–3.6% for the maximum oxytocin dose ranges of more than 20 mU/min and more than 30 mU/min. There was no significant risk association between time (in terms of both duration of oxytocin exposure and duration of labor) and UR risk [104].

The upper limit of 20 mU/min of oxytocin for use in VBAC trials is recommended with monitoring of oxytocin for both labor augmentation and induction.

Newer studies claim that labor induction and augmentation of labor have similar UR risks

when oxytocin exposure is considered. However, both induction and augmentation of labor are associated with an increased risk of UR compared to women who labor spontaneously. The initial cervical examination impacts this finding; an unfavorable initial cervical examination (<4 cm dilation) results in an increased risk of UR compared to spontaneous labor [105].

The benefit of intrauterine pressure catheter (IUPC) monitoring of uterine contractions in VBAC trials is unclear. Only a small case series failed to detect differences in fetal or maternal morbidity/mortality associated with UR when an IUPC was used instead of external tocodynamometry.

The intrauterine pressure catheter allows careful titration of oxytocin dosing, especially when maternal habitus limits the accurate external monitoring of uterine contractions in women undergoing a TOLAC.

### Cesarean Section and Induction of Labor

Labor induction is an increasingly common practice in the USA and accounts for at least 20% of births. While oxytocin is an effective drug in patients with favorable Bishop Scores, other pharmacological or mechanical agents are frequently utilized with an unripe cervix. Induction of labor after a prior CS appears to be associated with an increased risk of UR. The rate of UR that underwent labor induction after a single previous CS was 1.4–4% compared with 0.34–0.72% for women who had labored spontaneously [101, 102]. These findings suggest a fourfold to 12-fold increased risk of UR for labor induction after previous CS, dependent on the labor induction method.

### Prostaglandins

The use of misoprostol in women with prior cesarean delivery or major uterine surgery has been associated with an increase in UR and, therefore, should be avoided in the third trimester. (ACOG [82]).

Several studies found a several fold (3–5% compared to <1%) increased risk for UR using prostaglandins in gravidas who underwent a TOLAC [100, 101]. In contrast, the two studies did not show a significant difference, but in both studies, patients with the induction of labor had a higher percentage of spontaneous URs [106, 107]. Landon et al. reported no URs [88]. Although the study was underpowered to detect slight differences, the particular type of prostaglandin administered did not significantly affect the UR rate (misoprostol; dinoprostone; PGE2 gel; and combined prostaglandins) [88]. Misoprostol induction in patients with a previous CS results in the calculated risk of UR of 4.7% compared to 1% associated with a vaginal birth without misoprostol after a previous CS (fourfold increase) [108, 109].

Myometrial contractions in women with previous CS are associated with decreased total myometrial collagen and possibly connective tissue content. The incubation with misoprostol accentuates such an effect, while exposure to dinoprostone does not. The more pronounced contractile response and a decrease in collagen content observed with misoprostol may explain the higher incidence of UR observed in women with previous CS. They usually experience UR at the site of their old scar when treated with PGs for cervical ripening compared to other agents [21]. The milder effects of dinoprostone on collagen content suggest that it may represent a safer choice for labor induction in the setting of a previous CD [110].

Among women with a prior CS undergoing second-trimester abortion using misoprostol, the risk of UR was less than 0.3%. Women with a history of low-transverse segment CS and women induced with misoprostol alone were not found to be at risk for UR [111].

### Mechanical Methods

It is difficult to estimate the risk of UR with the use of mechanical methods of labor induction for cervical ripening because additional induction methods, such as oxytocin, are concomitantly used [112, 113]. The mechanical method with the mere use of a transcervical Foley catheter is a safe and effective method of VBAC in women

refusing the use of ecbolics [114]. A randomized controlled trial found that adding oxytocin to the use of a transcervical Foley catheter for labor induction does not shorten the time to delivery and has no effect on the likelihood of delivery within 24 h or the vaginal delivery rate [115].

Induction of labor with a transcervical Foley catheter alone may be a reasonable option for women undergoing a TOLAC with an unfavorable cervix.

### Cesarean Section with Previous Successful Vaginal Delivery

There is a protective association between previous vaginal birth on UR risk in subsequent attempts at vaginal birth after previous CS, with one-fourth to one-fifth of the risk [116]. In women with no prior vaginal delivery who underwent a TOLAC, there is an increased risk of UR with induction versus spontaneous labor (1.5% vs. 0.8%). In contrast, no statistically significant difference was shown for women with a prior vaginal delivery who underwent spontaneous TOLAC compared with labor induction (0.6% vs. 0.4%) [117].

### Cesarean Section with Subsequent Successful VBACs

A prior successful VBAC has a protective effect on the UR rate. Multiple potential explanations exist. The two most prominent are that a successful prior VBAC attempt assures that (1) the maternal bony pelvis is adequate to permit passage of the fetus, and (2) the integrity of the uterine scar under the stress/strain conditions during labor and delivery was adequate to result in vaginal delivery without UR. The UR rate decreases after the first successful VBAC, but there is no additional protective effect after that the UR rate was 0.87% with no prior VBACs, 0.45% for those with one successful prior VBAC, and 0.43% for those with two or more successful prior VBACs [118]. Pooled data indicate an increased UR rate of 1.4% in failed VBAC attempts that required a repeat CS in labor [88, 102].

### Interdelivery Interval

With an interpregnancy interval between CS and subsequent pregnancy of <18 months, UR is nearly three to four times more frequent than controls [119, 120]. A Canadian study on women who underwent a TOLAC after a single low-transverse CS found that 2.8% of patients who had an interdelivery interval of  $\leq 24$  months had a UR compared with 0.9% for those with an interdelivery interval of >24 months (OR 2.65) [121]. In a follow-up study, the same authors examined the risk of UR between 18 and 24 months. After adjustment for confounding factors, an interdelivery interval shorter than 18 months was associated with a significant increase of UR (OR 3), whereas an interdelivery interval of 18–24 months was not (OR 1.1) [122].

After a previous CS, an interdelivery interval shorter than 18 months but not between 18 and 24 months should be considered a risk factor for UR.

A prolonged interpregnancy interval might allow the previous CS scar to reach its maximal tensile strength before the scar undergoes mechanical stress and strain with a subsequent intrauterine pregnancy. A short interdelivery interval of  $\leq 24$  months and a single-layer hysterotomy closure are associated with a 5.6% UR rate—a rate threefold higher than patients without this combination. This is comparable to the rate of UR for patients undergoing a TOLAC with a previous classic midline CS scar [121]. There were no comparisons of single- or two-layer sutures.

### Single-Layer vs. Two-Layer Hysterotomy Closure

Myometrium closure techniques include interrupted, locked, and unlocked continuous sutures with single- or double-layer closure [123, 124]. Single-layer locked, continuous suturing, popularized in North America during the late 1980s, is part of the Misgav–Ladach technique developed by Stark et al. [124, 125]. A single-layer closure

might have several short-term benefits, including reduced operating time, decreased blood loss, reduced tissue disruption, and the reduced introduction of foreign suture material into the wound. Most studies [126, 127] compared a locked single-layer closure with a double-layer closure; it is, therefore, possible that many benefits are related to tissue strangulation by locked sutures, which results in better and faster hemostasis. However, few conclusions can be drawn about the short-term benefits of locked versus unlocked single-layer closures because studies comparing these two closure types are lacking [128]. One large randomized controlled trial did not confirm the reduced operating time and blood loss of a single-layer closure [129].

There is a four- to fivefold increased risk of UR after a previous single-layer uterine low-transverse closure (3.1%) compared to a two-layer closure (0.5%) for CS [130]. The recommendation is to avoid single-layer closure in women contemplating future VBAC delivery [130, 131]. Locked but not unlocked single-layer closures were associated with a higher UR risk than two-layer closures in women attempting a TOLAC [126]. An unlocked single-layer closure probably leads to better uterine scar healing, unlike locked sutures that increase pressure at the suture–tissue interface, leading to ischemic necrosis and impairing coaptation. Meanwhile, unlocked sutures provide coaptation, hemostasis, and wound strength in the immediate postoperative period [132]. Should the wound be exposed to additional pressure, an unlocked suture would provide more strength than a locked suture. Conclusions cannot be drawn because information on the suture type (locked or unlocked) for the first or second layer of a double-layer closure was unavailable. This parameter could have influenced the comparison between single- and double-layer closures. In addition, other factors such as suture material, the inclusion or exclusion of decidua in the uterine suture, and certain risk factors for UR, including fetal macrosomia, labor dystocia, and labor induction, were not considered. Decidua inclusion in sutures or eversion of the edges could result in a weaker scar and explain the difference between single-layer

locked, continuous, and double-layer closure [96, 133, 134].

Single-layer locked, continuous closure may increase UR risk in women attempting TOLAC in a future pregnancy. The risk of UR after an unlocked single-layer closure seems comparable to that after a double-layer closure.

Uterine closure with chromic catgut alone, irrespective of the number of layers, also resulted in a higher incidence of the abnormal lower uterine segment [96]. The rapid proteolytic degradation of chromic catgut, especially in the presence of infection, could be the reason [135].

### Multiple Cesarean Sections

Multiple CS carry a higher risk for UR than a previous single CS. Studies from 1993 to 2010 showed that UR risk in a subsequent pregnancy ranged from 0.9% to 6.0% (1/17–1/108). This risk is increased 2–16 times compared to women with only a single previous CS [136–138]. Women with a previous vaginal delivery were one-fourth as likely to have a UR as women without it (OR 0.26) [116]. The 2010 ACOG recommendation suggests that women with two previous low-transverse CS may be considered for TOLAC regardless of their prior vaginal delivery status [82].

### Placenta Percreta

The suggested incidence of abnormal placentation, including placenta percreta, varies between 1/540 and 1/93,000, with an average of 1/700. Recently, the incidence of placenta accreta has been rising due to the increased rate of CS [139]. Spontaneous UR due to placenta percreta is one of the most urgent obstetrical complications resulting in rapid exsanguination with high mortality. It is commonly seen in the third trimester and rarely in the second trimester [139]. It is rarely recognized as intrapartum and is very difficult to diagnose. The precise etiology of all cases of placenta accreta is unknown; however,

there are known factors that increase the risk. Most significant include scarring of the endometrial cavity with previous CS, uterine curettage, myomectomy, Asherman’s syndrome, iatrogenic uterine perforation, and advanced maternal age. These risk factors are frequent with IVF/embryo transfer. Placenta accreta is mainly caused by a combination of factors, and its occurrence is unlikely to be attributed to a single factor. A placenta percreta is common with a previously scarred uterus [140, 141]. It was present with an unscarred uterus but with previous uterine instrumentations (including IVF procedures) [142].

UR caused by placenta percreta mainly occurs during advanced pregnancy, with very few reports during the first trimester [143, 144]. In most URs during delivery, the affected site is the lower uterine segment; however, the fundus is the most common site in UR during the first trimester [143, 144].

**Sexual Intercourse**

Several case reports described the UR of the scarred uterus following sexual intercourse [77, 145]. The issue is whether it should be labeled spontaneous or traumatic URs. Also, it is unknown whether intercourse was accused as a cause in other reports of spontaneous UR without mentioning etiology.

**Gestational Age**

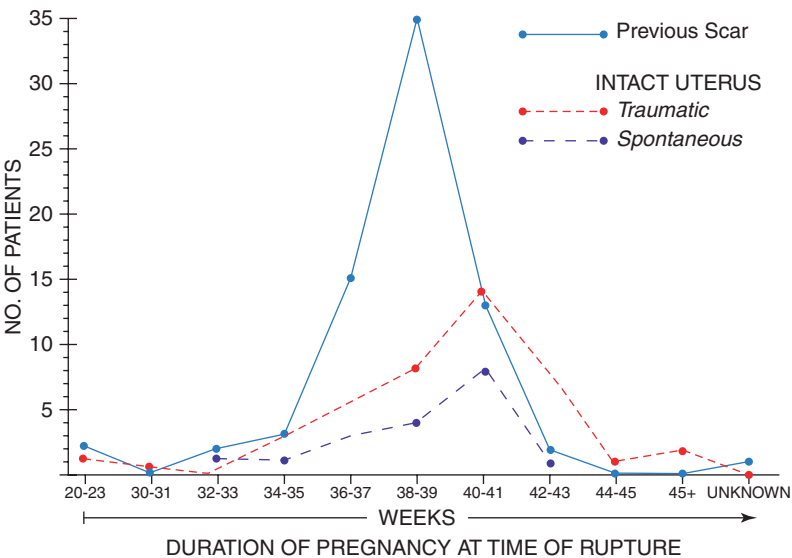
In both scarred and unscarred uteri, URs extremely rarely appear before 30 weeks of pregnancy. The incidence related to gestational age is presented in Fig. 10.7.

**10.1.5.2 Unscarred Uterus**

Back in 1845, Jackson confirmed M’Keever’s observations about risk factors for UR: “*I can fully bear out the opinion of Dr. M’Keever, in his Essay [147], that this dreadful accident occurs more frequently amongst the lower ranks than the higher; and I would suggest whether this result does not arise from the greater frequency of deformity of the pelvis as the consequence of rachitis or scrofula in the former class; and hence, it is highly probable that in large towns, where poverty and unhealthy occupants prevail, and especially where children are engaged in cramped or restrained positions, as in cotton factories, we shall find a higher ratio of this kind of difficult and dangerous parturition*” [148].

The anterior wall, particularly in the lower segment, is a typical site of rupture of an unscarred uterus [42, 43, 149]. Spontaneous rupture usually involves the lower segment and occurs during labor, while women with upper segment scars should deliver by CS before the onset of labor [150].

**Fig. 10.7** Rupture of the uterus related to the stage of gestation. Uterine rupture is the most frequent at or near term. (Reproduced with permission from [146])





### Oxytocin and Prostaglandins

For the stimulation of inert labor, the postulates for safe administration of oxytocin include (1) labor should be true, not false; (2) the inertia should be of the hypotonic variety; (3) wait until the cervix is two fingerbreadths dilated; (4) the oxytocin should be adequately diluted or divided and given over a safe period; (5) there should be no disproportion and no scar in the uterus; (6) constant attendance of medical staff is mandatory for administration a suitable anesthetic if the uterus should react violently; (7) the fetal heart should be frequently auscultated; (8) hesitate to use oxytocin if the patient has had more than four babies; (9) if there should be, any doubt, do not use it at all [22]. Feeney published the first cases of spontaneous UR receiving 5 units of oxytocin in 1956 [22].

Misoprostol (Cytotec®; Searle and Co, Chicago, IL) is a synthetic prostaglandin E1 (PGE1) analog. Owing to its uterotonic effect, it has been used as an abortifacient [151] for cervical ripening (placed in posterior vaginal fornix), labor induction, and the treatment of postpartum hemorrhage due to uterine atony [152]. UR with misoprostol induction has been reported in the English literature in 20 instances up to 2001. Seven ruptures occurred in the unscarred uterus, whereas 13 cases had CS scars [109]. In many cases, previous dilation and curettage, fetal macrosomia, external cephalic version, multiparity, shoulder dystocia, or oxytocin use might have contributed to UR. Misoprostol was used in a dose of 25–100 µg, or even 600 µg every 3–6 h with a maximum of four doses. An odds ratio of 2.7 for tachysystole with misoprostol compared to other medications used for labor induction was observed [153].

PGE2 (dinoprostone) is a potent oxytocic agent, and rupture of the unscarred uterus has been reported with vaginal and intracervical applications [29, 75] in doses up to 6 mIU/min. PGE2 should be used cautiously, particularly in multiparous patients and oxytocin use. Uterine hyperstimulation was not observed, and UR occurred >4 h after administration [12].

### Assisted Vaginal Delivery

Application of external force in the second stage of labor [9], vacuum forceps, and breech extrac-

tion are possible causes of UR [75]. Midforceps delivery and breech version extraction have been implicated as potential causes of UR [154]. Whether the manipulation results in UR is unclear.

### Parity, Age, and Race

*High multiparity carries with it certain inherent risks ... it can be very unforgiving of any carelessness, incapacity, or neglect.*

(John Kevin Feeney, 1935)

There could be a significant difference in the influence of parity on the term and preterm UR. The high parity, first observed by John Kevin Feeney (Professor of Gynecology and Obstetrics at University College Dublin and Master of the Coombe Hospital in Dublin) in 1953, is recognized as a major risk factor of spontaneous UR in an unscarred uterus [22, 155]. The uterus may have been weakened by thinning and stretching muscle fibers during labor, especially with aging and repeated childbearing [12]. The mean parity at the time of UR is 5–6 [156, 157]. Some reported that 56–75.6% of URs occurred with a parity of 1–4 and 38% with a parity of 5–9 [158, 159]. The precise influence of parity comes from the reports of cumulative incidence of the scarred and unscarred uterus [43, 146]. Some claim that the incidence rises until the third delivery and then decreases [43]. Grand multiparity predisposes to malpresentation and unstable lie, a significant risk factor for UR [64, 66]. Grand multiparas attend antenatal clinics sparsely (due to heavy domestic commitments), and consequently, malpresentation is diagnosed late during labor. Nevertheless, with proper antenatal care, modern obstetrics, and advanced neonatal services, there is no difference in outcome between grand multiparous women and women with low parity [160]. Only 0.005% of UR among 39,529 multigravidas developed without previous uterine scar [69]. Uterine overdistension from twin pregnancy was not proven as a risk factor. Fetal weight in singleton pregnancy is a risk only when it contributes to cephalopelvic disproportion [41]. Age and parity are interrelated risk factors.

Preterm UR is most common in primigravida, resulting from traumatic events due to uter-

ine instrumentation [23]. Congenital abnormalities, connective tissue disorders, and abnormally invasive placenta are known risk factors for UR in a primigravida [62].

Women older than 35 and having their fifth or later birth are at the greatest risk for spontaneous term UR.

The peak incidence differs from country to country and depends on the average age of the first pregnancy and the number of pregnancies. Therefore, some claim peak incidence in the 26- to 35-year age range [158], while others showed a peak incidence in the 25- to 29-year age group. In Qatar, where repeated pregnancies continue into middle age, 56.9% of URs were grand multiparas (para 5 or more), and 39% were over 35. The factors contributing to a rupture of the unscarred uterus are presented in Table 10.1. Connective tissue diseases [161] may also induce UR. In some cases, the gravid UR has no apparent cause even before labor [15, 162].

A major factor for UR is obstructed labor. Black African women have a high incidence of the contracted pelvis [163].

An unscarred prelabor primigravid uterus can show a very thin uterine wall, compatible with incomplete UR, without apparent etiological or risk factors. There have been 36 [164] and 22 [165, 166] cases of primigravid URs found over the last 65 years (1946–2013). Of 21 cases found by Matsubara et al., 15 were reported in Nepal [167], with all ruptures occurring after labor duration of >48 h, and 12 had received no antenatal care. Of all these 58 (36 + 21 + 1) cases, 55 had some discernible etiological or risk factors for UR, including a history of uterine surgery, congenital uterine anomaly, adherent placenta, labor, or oxytocin or prostaglandin use [161, 164, 166]. The etiology was indiscernible in the remaining two [168, 169], while in one, there was a history of curettage [165], but without the evidence being a cause.

## Congenital Uterine Anomalies

Congenital uterine anomalies affect approximately 1/200 women [170]. In such cases, the walls of the abnormal uteri tend to become abnormally thin as pregnancies advance, and the thickness can be inconsistent over different aspects of the myometrium [171], predisposing it to rupture (Fig. 10.8). The reported incidence of UR in women with congenitally malformed uteri is 8% compared to 0.61% in those with normal uteri attempting VBAC [173]. Cases of UR in women with uterine anomalies involved labor induction with prostaglandin E2. In contrast, a study of 165 patients with Müllerian duct anomalies who underwent spontaneous labor after one prior CS reported no cases of UR [174]. In this study, 36% had only a minor uterine anomaly (arcuate or septate uterus), and 64% had a major uterine anomaly (unicornuate, didelphys, or bicornuate uterus). Moreover, only 6% with Müllerian duct anomalies underwent induction of labor.

### Rudimentary Horn

See Chap. 9.

### Uterine Sacculation

A thin uterine wall resulting from uterine sacculation [175, 176] may induce UR. Uterine sacculation is a transitory pouch or sac-like structure developing from a portion of the gravid uterus [175]. The typical form of sacculation results from an incarcerated retroverted uterus [175,



**Fig. 10.8** Fundal uterine rupture in the left part of the bicornuate uterus in a 12-week pregnancy. (Reproduced with permission from [172] under the CC BY Attribution License)

[176]. A ventrally located cervical ostium and vagina may cause physicians to suspect this diagnosis. In this condition, the anterior uterine wall becomes stretched and thin. Other conditions, such as previous surgery, a primary myometrial defect, uterine malformation, or placental abnormalities, are listed as possible causes of uterine sacculation [175].

### Uterine Diverticulum

The diverticulum can result from a developmental malformation (true diverticulum) or weakening of the uterine wall from prior uterine surgery (iatrogenic or secondary diverticulum) [177]. A uterine diverticulum is frequently misunderstood and reported as uterine sacculation [177]. On the other hand, uterine sacculation is typically a larger outpouching that contracts after delivery. It occurs during pregnancy as the uterus is distended by the destruction of the uterine wall by trophoblastic tissue [177]. The hypothesis is that abnormal development of the paramesonephric duct may cause a congenital uterine deformity, leading to the formation of the diverticulum [178]. The uterine diverticulum has a narrow connection with the uterine cavity and a thicker wall than uterine sacculation [177]. While uterine sacculation is usually observed during pregnancy [175], the diverticulum is usually detected in nonpregnant women. Uterine diverticula as complications during pregnancy are rare. An asymptomatic diverticulum in pregnancy indicates elective CS before uterine contractions and labor. Extreme caution is needed because there are cases of UR before uterine contractions as a start of labor [177, 179]. Also, if the gestational sac is implanted in a diverticulum [178], there is a significant risk of UR and other obstetric complications, and the pregnancy should be terminated.

### Genetic Susceptibility for Rupture

Loeys–Dietz syndrome is caused by heterozygous mutations in the genes encoding type 1 or 2 transforming growth factor  $\beta$  receptor (TGF- $\beta$ RI/2). It carries a risk of gravid UR and the arteries during pregnancy or in the immediate postpartum period and damage to the vagina, the perineum, and the colon [180].

### Antenatal Care

Prenatal care in some undeveloped countries such as Yemen or Uganda is indigent. Only 44% of pregnant women had ever been to any prenatal clinic, with visits ranging from one to four during a pregnancy. Women visit antenatal clinics mostly when they encounter complications and rarely for routine antenatal care (13%). In Yemen, 56% of pregnant women have never had antenatal care. Home delivery is still typical. About 78% of women deliver at home, 16% at state hospitals, and 5% at private hospitals. Home deliveries are usually attended by midwives with minimal training or relatives with some labor experience. Some of the women will still deliver at home alone [41]. In Uganda, the majority (67%) of the women did not attend antenatal care [20].

### Epidural Anesthesia

Epidural anesthesia has been linked to UR [60, 181]. Plauché et al. suggested that “the propriety of the sitting position for the induction of epidural or spinal anesthetic procedures for delivery created an increase in intra-abdominal pressures that may be sufficient to produce a uterine rupture” [181]. However, epidural use is low in patients with UR, ranging from 6% to 21% [60, 181, 182].

### Uterine Fibroids

Fibroids are associated with numerous pregnancy complications (see Chap. 12), including pain, miscarriage, premature labor and delivery, malpresentation, and placental abruption [183–185]. Approximately 10–40% of complications are in this group [186]. UR occurs after myomectomies, not with uterine fibroids. Uterine fibroid rupture during pregnancy or puerperium presents with bleeding. Two cases of uterine fibroid rupture with UR were detected during labor [187, 188].

### 10.1.5.3 Operative Procedure

#### Prepregnancy Uterine Myomectomy

Most URs with myomectomy scars occur during the third trimester of pregnancy or labor [189–194], with several cases during the second [195–

[198] or even the first trimester [199]. Some claim a 3–4% UR rate in women with scars from a previous myomectomy—open or laparoscopic [146, 189]. Such reports often do not delineate the important factors for assessing the risk of subsequent UR (e.g., number, size, and locations of leiomyomas; number and locations of uterine incisions; entry of the uterine cavity; and type of closure technique). The risk is significantly lower with these factors included in the analysis, 0.26–1% [189, 190].

Because the neuropeptide substance P and vasoactive intestinal peptide in the pseudocapsule of uterine myomas may affect wound healing and myometrial function in a subsequent pregnancy, the pseudocapsule with neurovascular bundle should be respected to prevent damage by excision or extensive coagulation [200, 201]. Therefore, intracapsular laparoscopic myomectomy, which preserves these neuropeptides and enables proper myometrial healing, is recommended [202]. Compared to open myomectomy, laparoscopic myomectomy could increase the risk because the rate of 2-layer closure is lower, with higher use of tissue coagulation [201, 203]. Other studies did not find the influential role of laparoscopic myomectomy in association with UR [204]. Other UR preventive measures after prepregnancy myomectomy include (1) elective CS for numerous and deeply placed fibroids, (2) opened endometrium, (3) accurate apposition of the wound edges and hemostasis had not been secured, (4) recovery had been complicated by fever, and (5) the placenta has been implanted on ultrasound (US) examination upon an endometrial scar [22]. An interval of contraception after myomectomy to ensure adequate wound healing might be necessary. Evaluation of changes in uterine structure (resolution of hematoma, absorption of suture materials, decrease in scar size, etc.) during the recovery process after myomectomy using MRI [205], US [206], and 3D Doppler US [207] leads to the conclusion that the wound healing process completes by 3 months. Cases 8 years after laparoscopic myomectomy exist [208], meaning that prolongation of contraception alone may not reduce the risk of UR and such an interval is not a definitive risk factor for

UR [209, 210]. In conclusion, at least 3 months is needed for uterine wound healing, while some recommend 6 months of contraception [201]. The most rigorous recommendation can follow the recommendation that pregnancy and vaginal delivery are safe 18 months after CS.

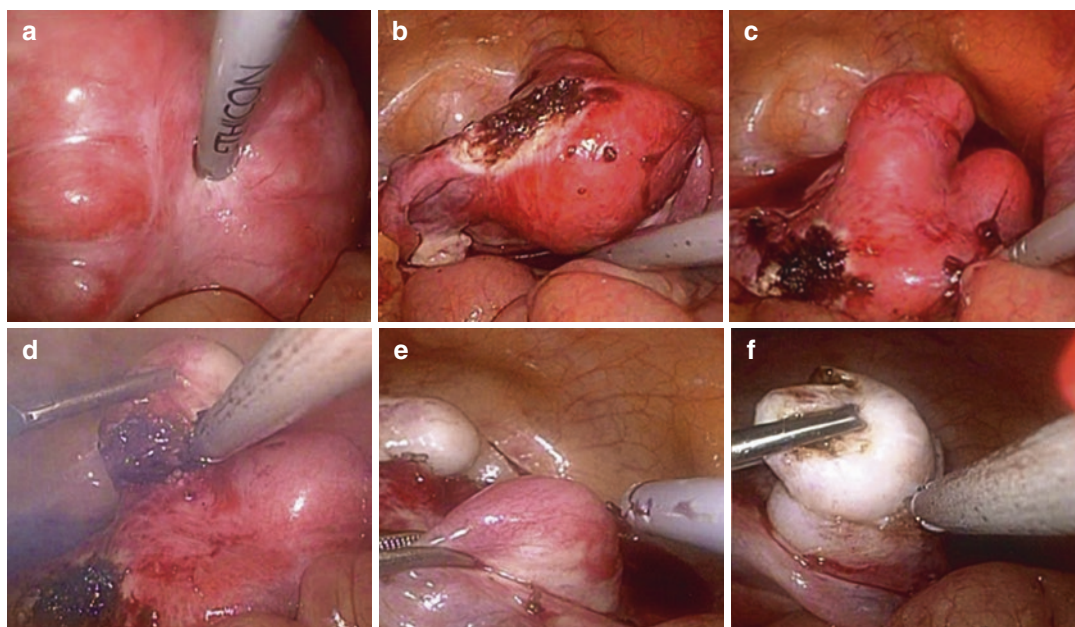
These measures (including vasoconstrictors instead of coagulation) can minimize UR [192, 202, 204, 211–215]. These outcomes should be cautiously analyzed because some studies did not find UR, but the uterine dehiscence rate was 1.8–4.9% [209, 216]. Prepregnancy myomectomies should be recorded, so that if the UR or uterine dehiscence occurs, the locations could be compared (Figs. 10.9 and 10.10).

Women who have undergone laparoscopic myomectomy would best avoid multiple pregnancies because of the potentially increased risk of UR. This is extremely important when assisted reproduction techniques are used in these women; single embryo transfer would be preferable, whereas intrauterine insemination could be managed without any ovarian stimulation [203].

### Medical Abortion

Medical abortion was started in the late 1980s, becoming more widely used in the late 1990s, with mifepristone and misoprostol being the most used. It came as an alternative to dilation and curettage, which caused more complications, resulting in 50,000–100,000 maternal deaths yearly [217, 218]. No randomized controlled trial has been powerful enough to compare medical and surgical abortions concerning the adverse effects. Misoprostol (partial progesterone receptor agonist which also antagonizes cortisol action competitively on the receptor level) alone for the termination of pregnancy was described in 1994. It has been used widely in the normal uterus [217, 218]. The absence of previously reported cases of gemeprost-associated UR may reflect the rarity of this pregnancy termination method in the second trimester. Initially, higher doses were admin-





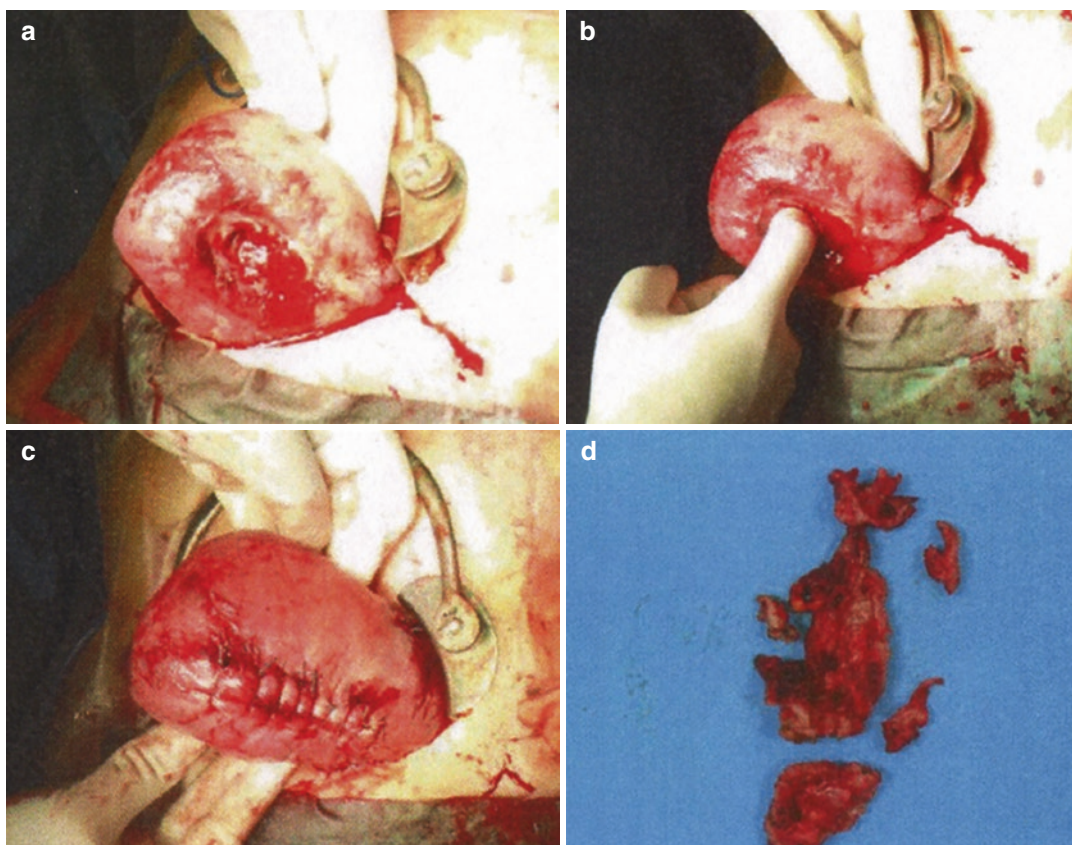
**Fig. 10.9** Sixteen months prepregnancy laparoscopic myomectomy. (a, b) The subserosal myoma in the fundus was removed by cutting its narrow stalk. (c, d) another subserosal myoma on the anterior wall was removed by

cutting its stalk. (e, f) the intramural myoma on the anterior wall was enucleated. (Reproduced with permission from [201])

istered, and the conclusion was that smaller doses might lessen the risk of uterine hypertonus and decrease the risk of UR [219]. The additional risk factor in such cases is scarred uterus [220–222], but there are even cases with an unscarred uterus [109, 223]. The systematic review from 2009 found a seven times higher incidence of UR in the scarred uterus (0.28%) in comparison with the unscarred uterus (0.04%), but the authors found the incidence acceptable [111]. UR in an unscarred uterus is possibly related to the dose, dose interval, gestation, and parity. Based on the pharmacokinetics of misoprostol, a dosage interval is 6 h (range 3–12 h) [224]. UR occurred in one case with a lower accumulated dose of misoprostol (1200 µg/30 h) than in some reported regimens (2400 µg/24 h) [224]. A case of spontaneous UR of the unscarred uterus in the first trimester using mifepristone/misoprostol for medical termination of pregnancy exists [225]. Corticosteroid therapy is a contraindication to mifepristone (but not misoprostol) because of the glucocorticoid antagonistic effect. Whether pro-

longed corticosteroid therapy can result in a weakened myometrium susceptible to rupture remains to be determined. The incidence of UR among women with a prior CS during second-trimester pregnancy termination with prostaglandin E2 or oxytocin is 3.8% [226]. The risk is even higher when oxytocin is used with prostaglandins [227]. There was no set regimen protocol for intravaginal misoprostol in second-trimester pregnancy termination. Mostly the initial dose was 400 µg repeated every 4–6 h, up to a maximum of 1200–1600 µg/24 h. Some studies have augmented misoprostol with either oxytocin or mifepristone [220, 223, 226]. FIGO has recommended the protocol for second-trimester pregnancy termination with 100–200 µg intravaginal misoprostol, repeated every 6 h till a maximum of four doses/24 h [227]. Its use should be with care in a previously scarred uterus. Four cases of rupture of an unscarred uterus in the second trimester following MTOP were reported. Only two of these cases used mifepristone and misoprostol [228]. The other women found do





**Fig. 10.10** Uterine rupture was identified during the emergent Cesarean section at 33 weeks of gestation (the same patient from Fig. 10.9). (a, b) The myometrial defect reached the endometrial cavity. It was  $2 \times 3$  cm in size and located near the right uterine horn on the anterior uterine

wall. (c) Debridement and 2-layer myometrial suturing. (d) Macroscopic picture of resected tissues in the ruptured site of the myometrium. The pathological diagnosis of the removed myometrial specimen was focal myometrial necrosis. (Reproduced with permission from [201])

not follow the MTOP protocol but contain information relevant to this case. The first was an MTOP using mifepristone and gemeprost. The rupture was found by US the morning after commencing prostaglandins [229]. The second case was a grand multiparous patient [222]. An US found the UR following one dose of misoprostol (200  $\mu$ g) followed by oxytocin 12 h later. Although high doses of prostaglandins are a known risk factor, the above two women were treated for over 24 h, raising the possibility that the duration of prostaglandin treatment is a risk factor. Other agents, such as ethacridine lactate, have been linked to UR, although this is very rare, and the case was related to the second tri-

mester [230]. Cases of UR have been reported involving small doses of misoprostol. One case involved an endocervical rupture in the second trimester following two doses [231]. Another was a scarred uterus [232], and a similar case was the first-trimester UR following one dose of misoprostol in preparation for surgical termination [199].

There is no evidence that pretreatment with mifepristone might increase the chance of UR. The chance might be reduced as mifepristone increases cervical compliance; however, as it increases uterine sensitivity to the action of exogenous prostaglandins [229], the risk–benefit is unknown. Previous CS could be a risk factor

for UR. One trial of second-trimester abortion using misoprostol in 720 women with one or more previous CS concluded that misoprostol was not associated with an excess of complications compared with women with unscarred uteri [233].

### **Uterine Curettage**

See Sect. 18.3.

### **Salpingectomy**

The ectopic pregnancy site, type, and quality of suture material, suturing technique, mono- or bipolar electrocautery, and the gynecologist's experience influence outcomes after laparoscopic Fallopian tube resection [234, 235].

To decrease the risk of long-term complications from a ruptured tubal pregnancy localized near the cornual region, using additional reinforcing sutures during laparoscopy appears to be more appropriate management than electrosurgery alone since cautery-induced thermal injury may compromise the myometrial tissue [236]. However, additional sutures in the cornual region may be associated with a risk of myometrial ischemia. Therefore extensive suturing should be avoided. For unruptured tubal pregnancy, conservative therapy with methotrexate or laparoscopic salpingostomy is the methods of choice (see Sect. 9.1.7.3) that can prevent severe complications in subsequent gestations [237].

Apart from the surgical approach, the time between the surgical removal of a Fallopian tube and conception is important. It was <12 months in 67% of the analyzed URs in the group of non-ectopic pregnancies. Interstitial pregnancy was the cause in all cases. However, it is impossible to determine the safe interval between conception and salpingectomy with a high degree of certainty, and the risk of UR during subsequent pregnancy cannot be excluded entirely after several years [238].

### **Uterine Artery Embolization**

Except for uterine artery embolization, described cases with UR had additional risk factors for which uterine artery embolization was indicated. Most include (resected) uterine myomas or

abnormal placentation during pregnancy with UR [239–241].

## **10.1.6 Prevention**

### **10.1.6.1 Scarred Uterus**

The most direct prevention strategy for minimizing the risk of pregnancy-related UR after CS is to minimize the number of patients at the highest risk. The salient variable is the threshold for a tolerable risk. Although this choice is arbitrary, the safety threshold is 0.5% (1/200). Therefore, the categories of patients that exceed this critical value are those with previous:

- Multiple CS,
- Classic midline CS,
- Low-vertical CS,
- Low-transverse CS with a single-layer hysterotomy closure,
- CS with an interdelivery interval of <2 years,
- Low-transverse CS with a congenitally abnormal uterus,
- CS without a previous history of a successful vaginal birth,
- CS with either labor induction or augmentation,
- CS in a woman carrying a macrosomic fetus weighing >4000 g,
- Uterine myomectomy.

Accurate prediction of UR would be extremely valuable, as it would allow women at low risk to proceed with a TOL, whereas women at high risk for UR could undergo a planned CS. Thinning in the lower uterine segment measured by US predicts UR's complete rupture or scar dehiscence at birth during TOLAC. A full lower uterine segment thickness cutoff of 3.1–5.1 mm and a myometrium thickness cutoff of 2.1–4.0 mm provided a strong negative predictive value for the occurrence of a defect during TOLAC. A myometrium thickness cutoff between 0.6 and 2.0 mm provided a strong positive predictive value for the occurrence of a defect [242]. The interobserver agreement is that the lower uterine segment thickness should be measured by transvaginal US [243].

### 10.1.7 Clinical Presentation

The prevalence of Müllerian duct malformations in the general population and the population of fertile women is estimated to be 4.3%, and in infertile patients, approximately 25%. The septate uterus is the most common anomaly (35%), followed by the bicornuate uterus (25%) and the arcuate uterus (20%) [244]. These malformations remain asymptomatic until the patient reaches reproductive age. Such anomalies result in an increased rate of infertility, miscarriage, recurrent pregnancy loss, preterm labor, and other obstetric complications. Clinical presentation varies from asymptomatic to vague complaints of mild lower abdominal pain with gastrointestinal upset and its severest form of acute abdomen with hemorrhagic shock. Women with a noncommunicating uterine horn may present after menarche with progressive abdominal pain caused by hematometra, hematosalpinx, and endometriosis. However, many women remain asymptomatic.

#### 10.1.7.1 Symptoms

The symptoms and signs of UR largely depend on [22] the following:

- Time of occurrence (pregnancy, early or late labor),
- Cause,
- Duration,
- Site,
- Type,
- Degree,
- Extent,
- The amount of intraperitoneal spill,
- The size of the blood vessels involved,
- Complete or partial extrusion of the fetus and placenta,
- The intensity of retraction of the uterine muscle.

Sudden, severe, shearing abdominal pain with the absence of fetal heart sounds, cessation of uterine contractions, and recession of a present-

ing part, combined with vaginal bleeding and shock, is a classical presentation [154]. Overall, only 45% of the cases reviewed have typical symptoms and signs of UR [39, 45, 54, 154, 159, 245–248]. The most common presentation is fetal distress, mainly as a nonreassuring fetal heart rate pattern with variable deceleration at a time in labor when they are not characteristically seen [82, 154]. Fetal distress occurs in 81% before abdominal pain or vaginal bleeding [182].

#### Pregnancy

Common symptoms and signs are abdominal pain and tenderness, shock (faintness, pallor, and tachycardia), vaginal bleeding, fetal distress, manifested by fetal bradycardia, absence of fetal movement, undetectable fetal heartbeat, palpable fetal body parts, cessation of contractions, and signs of intraperitoneal bleeding. Severe abdominal pain is present in 14% of patients, shock in 10–21.3%, bleeding in 16.8%, the disappearance of fetal heart sounds in 8.9%, and cessation of contractions in 5.6% [149, 247]. Epigastric pain, shoulder pain (right-sided or bilateral), abdominal distention and paralytic ileus, hypertonic uterus, altered uterine contour, and fluid thrill are less commonly associated with UR. Hematuria and vernixuria (vernix caseosa in urine) are additional signs resulting from a rupture extension to the bladder [249].

#### Labor and Postpartum

UR during labor is associated with cessation of labor pain, the recession of presenting fetal body parts, cervical lacerations, and vaginally palpable uterine defects. One of the pathognomonic signs of constriction–ring dystocia is that, despite a painful, colicky contraction originating and felt in the upper part of the uterus, no impulse of descent or pressure is imparted to the presenting fetal head below. Downward contractile impulse is cut off by the gap in the continuity of the muscle fibers at the rupture site. After rupture, the uterus continues to contract above, but the fetal head below remains immobile to the examining finger during a contraction [22]. This phenomenon partly depends on the degree and extension of UR and the associated partial or complete expulsion of the fetus in the peritoneal cavity.

The most common sign is the sudden appearance of fetal distress during labor. Up to 81% of patients with UR during labor have evidence of fetal distress before bleeding or abdominal pain [182] and fetal heart abnormalities in 43.5% [57]. The observation of sudden fetal heart irregularity in laboring women is a dangerous sign [70].

Postpartum bleeding is present in 24%, while postpartum abdominal pain, distention, and ileus are present in 14% [149]. A large blood clot evacuated with the spontaneous exit of the placenta, especially in patients on uterotonics or prostaglandins for induction of labor, should raise the suspicion of UR [109]. Another suspicious sign is bloodstained liquor after the rupture of membranes [187].

### Scarred Uterus

The symptoms and signs of UR in patients with scarred uterus differ from patients without a uterine scar [246]. UR at a previous uterine scar site is typically less violent and dramatic than a spontaneous or traumatic UR because of its relatively reduced vascularity. Hypogastric tenderness is the most common sign in women with a previous uterine scar. In women without a scar, shock is the most common sign, followed by uterine bleeding, severe abdominal pain, and easily palpable fetal parts. Severe abdominal pain is common in both groups of women with and without a uterine scar.

### Incomplete and Silent Rupture

At first, *quiet*, *silent*, or *occult rupture* occurs without the symptoms and signs ordinarily associated with UR. Diagnosis may be difficult or unduly delayed, and unless the possibility of UR is suspected, it may be missed. In quiet rupture, there is the uncomplaining multipara in labor or the patient whose CS scar is stretching and finally yields in either pregnancy or labor. Nothing dramatic happens, but an increase in the pulse rate, pallor, perhaps slight vaginal bleeding, and the patient complains of some pain is present. Contractions may continue unaltered, but the cervix fails to dilate further—an essential sign [22]. Uterine tenderness on internal examination is present [250]. UR as the incidental finding is

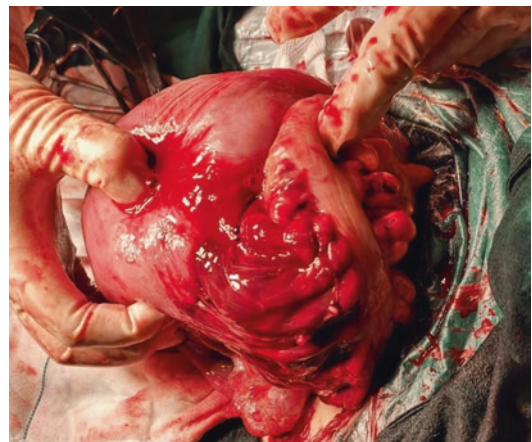
present in 4.5% [247]. Cases that presented as puerperal sepsis have shown to be unrecognized UR.

Silent antepartum UR is usually associated with a previous uterine scar from CS, myomectomy, or uterus perforation at the time of curettage. Antenatal spontaneous silent rupture of the intact uterus is exceptionally rare [162, 169, 250, 251], without predilection of UR location. High parity is common.

### Delayed Presentation

Delayed presentation with abdominal pain and minimal or absent other symptoms and signs is possible if the UR is “covered.” The rupture site may be covered from the outside by the small [252] or large intestine [253] or from the inside by fetal legs [254], preventing massive bleeding. Therefore, vital signs and laboratory data could be stable. The external covering of UR may prevent amniotic rupture or amniotic cavity protrusion, explaining the initial absence of a fetal heart rate pattern indicative of cord issues (Fig. 10.11).

Another delayed presentation is during early postpartum. The condition is not suspected or diagnosed until the patient has become established upon slow but progressive postpartum bleeding. The UR, which does not cause symptoms until the early postpartum period, is impor-



**Fig. 10.11** Defect of the posterior wall of the uterus adhered to the sigmoid colon, hematoma on mesentery, and active bleeding on the rupture site. (Reproduced with permission from [253] under the CC BY 4.0)



tant because traumatic bleeding may be attributed to atony of the uterus and collapse to so-called obstetrical shock [22].

### Epidural/Spinal Anesthesia

Epidural analgesia rarely masks the symptoms and signs of UR [60, 182, 255]. The sudden development of “breakthrough pain” under epidural analgesia may improve the specificity of abdominal pain as a symptom of UR in patients attempting vaginal birth after previous uterine surgery [82].

#### 10.1.7.2 Physical Examination

A physical examination reveals tenderness in the middle of the lower abdomen with or without guarding. Vaginal bleeding can be present. Blood pressure depends on the severity of uterine bleeding, and the patient can be hypotensive with an increased pulse rate. A lump (expelled fetus) could be palpated in a hospitalized patient with new-onset UR without the presenting part [154]. Shoulder pain (*Kehr's sign*) is a valuable sign of intraperitoneal blood in the subdiaphragmatic region. Even a small amount can cause this symptom, but it is important to realize that it may be 24 h or longer after the bleeding has occurred before blood will track up under the diaphragm. Also, some acute massive intraperitoneal bleeding may not initially have shoulder pain. Sooner or later, however, shoulder pain will usually appear. In doubtful cases with slow intraperitoneal bleeding for 2 or 3 days, such referred pain has great diagnostic value.

With sufficient cervical dilation, a vaginal examination may reveal intestinal loops, parts of the greater omentum in the uterine cavity, or a defect of the (lower) uterine segment [109, 256]. Considerable abdominal distension compressing the thoracic cavity results in dyspnea. Postpartum fever  $\geq 38^\circ\text{C}$  after CS is associated with an increased risk of UR during a subsequent trial of labor [257]. Antepartum hemorrhage (APH) often indicates UR [33] and may be associated with shoulder tip pain due to hemoperitoneum. APH is present in 33% of posterior URs [32]. With posterior UR, bleeding may be concealed, where signs of hypovolemia develop, with a

large, concealed hemoperitoneum [29, 30]. Maternal pulse and blood pressure could remain within normal limits despite massive UR, demonstrating the potentially misleading capacity for compensation in an otherwise fit patient. Women reported persistent abdominal pain in 33% of posterior URs [29, 32]. A hard mass can be palpated if the fetus is partly or entirely outside the ruptured uterus, especially if the UR is on the anterior wall [8].

### 10.1.8 Diagnosis

*It is a worthy subject of an obstetrical truism - that is, if a multiparous patient, in pregnancy, in labour, or in the early postpartum period, should develop constitutional or local (abdomino-pelvic) signs and symptoms for which there is no ready explanation, then rupture of the uterus should at least be suspected.*

(John Kevin Feeney, 1956 [22])

#### 10.1.8.1 Laboratory Findings

Only 30% of patients are diagnosed with UR preoperatively [70, 158]. Laboratory findings show lowered serum hemoglobin levels, and the exact value and dynamics of its decrease depend on the intensity of uterine wall bleeding. Suspicion of placenta accreta/percreta arises in the case of an unexplained elevation of alpha-fetoprotein [258].

#### 10.1.8.2 Abdominal Ultrasound

A transvaginal and transabdominal US is helpful for the direct and indirect findings of UR. Direct signs are a thin wall with bulging of fetal parts (Fig. 10.12) or visualization of the rupture. The fetus can be partly (Fig. 10.13) or entirely out of the uterus (Fig. 10.14). Indirect signs include free peritoneal fluid (blood), especially in the pouch of Douglas, extraperitoneal hematoma, intrauterine blood, empty uterus, and gestational sac above the uterus (Fig. 10.15), and large uterine mass with gas bubbles [8, 259, 260]. Congenital uterine anomalies or acquired uterine changes raise the suspicion of UR.

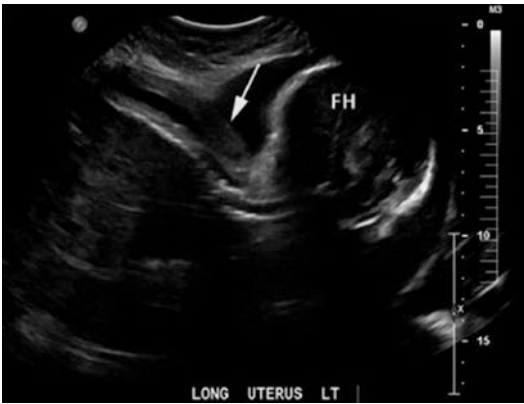
#### 10.1.8.3 Abdominal CT

An abdominal CT is indicated in uncertain cases such as intestinal adhesions over UR, delaying





**Fig. 10.12** An abdominal ultrasound of the uterine wall and the minor fetal part. A *small arrow* indicates a thin uterine wall, which is slightly bulging. Beneath the thin uterine wall, a minor fetal part (*large arrow*) is visible and palpable mass through the abdomen. (Reproduced with permission from [8] under the CC BY 2.0)



**Fig. 10.13** Unrecognized edge of the uterine rupture (diagnosed initially as synechiae (*arrow*) due to the history of uterine curettage) and the fetal head already extruded through the uterine defect. (Reproduced with permission from [165])



**Fig. 10.14** Abdominal ultrasound shows a contracted uterus with fetal extremities and amniotic sac outside the uterus. (Reproduced with permission from [259])

diagnosis. It is seen as a focal disruption of the myometrium with the hemoperitoneum. Other signs, as found on US (see Sect. 10.1.8.2), such as fetal parts or hemoperitoneum outside the uterus, can be visualized (Figs. 10.16, 10.17, and 10.18).

#### 10.1.8.4 Abdominal MRI

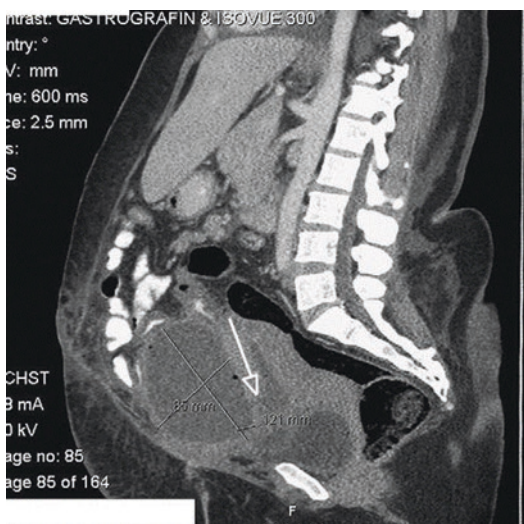
US diagnosis relies on nonspecific, secondary signs such as free fluid or hematoma formation, while MRI allows the visualization of the uterine wall defect or tear with higher accuracy [262]. MRI may also be less uncomfortable for the patient with a tender abdomen.



**Fig. 10.15** Abdominal ultrasound shows a contracted uterus, endometrial stripe, and no intrauterine gestation, with the placental tissue above and bladder to the right. (Reproduced with permission from [259])



**Fig. 10.16** Contrast-enhanced abdominopelvic CT shows a defect in the anterior wall of the uterus (*arrow*) and fluid collection with wall enhancement and adjacent fluid collection 2 weeks after elective Cesarean section. (Reproduced with permission from [261])

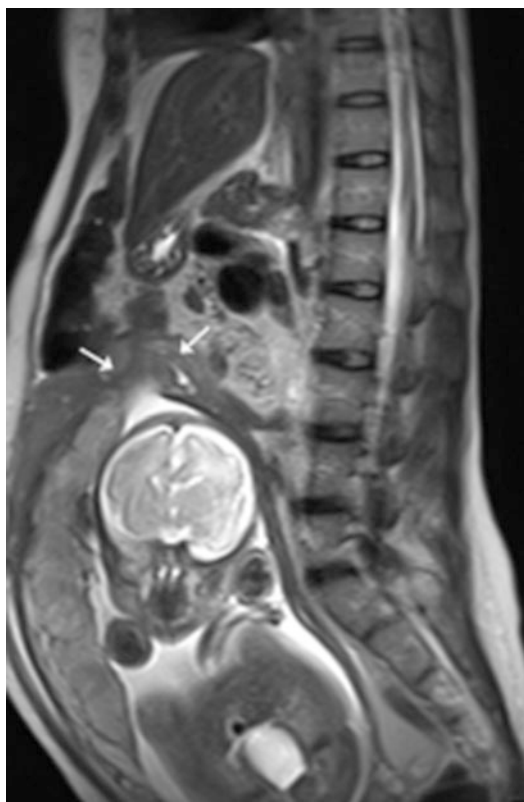


**Fig. 10.17** Axial CT of the abdomen (the same patient as in Fig. 10.16) shows fluid collection anterior to the uterus (arrow). (Reproduced with permission from [261])



**Fig. 10.18** Abdominal CT shows an empty uterus (arrow) and the fetus (F) outside of the uterus, denoting uterine rupture. (Reproduced with permission from [165])

The MRI appearance consists of a focal myometrial defect: (1) filled with hematoma and an associated hemoperitoneum (Fig. 10.19) and (2) protruding amniotic cavity (Fig. 10.20) or protruding placenta [264]. The characteristic sign is the *shower cap sign* [264]. UR is a surgical emer-



**Fig. 10.19** A female in the third trimester with prior cesarean delivery. Sagittal T2WI shows a focal disruption at the uterine fundus (arrows) with associated hematoma. No part of the fetus protruded into the abdominal cavity [263]

gency, and MRI should only be considered when the diagnosis is inconclusive, and the patient is hemodynamically stable [265].

Scar dehiscence results in an extensive fluid collection with air bubbles in the bladder flap as a sign of local infection. The differential diagnosis includes bladder flap hematoma, endometritis, and regular CS incision changes, better depicted with MRI than CT. MRI may provide a preoperative diagnosis of uterine sacculation [176] or uterine diverticulum [177].

#### 10.1.8.5 Cardiotocography

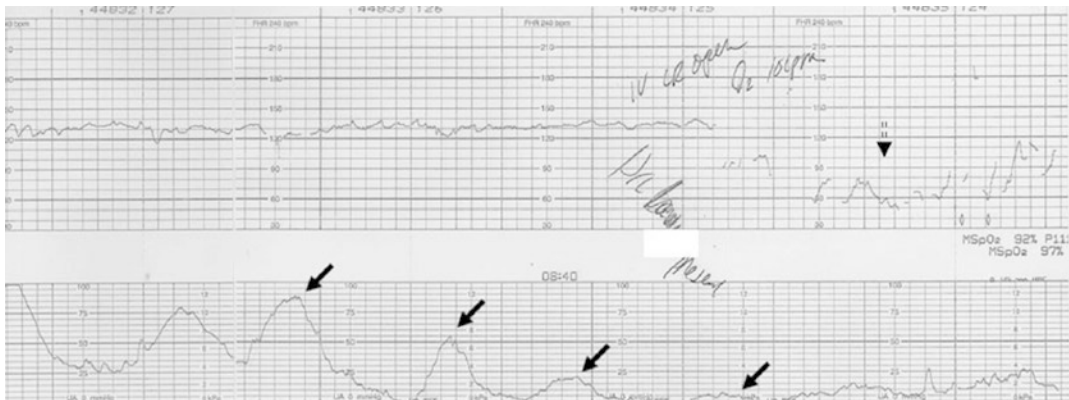
CTG abnormalities are associated with 55–87% of URs [266]. Other recognized signs of UR include loss of station of presenting part and new inefficient contractility [267].



**Fig. 10.20** Abdominopelvic MRI (T2WI, coronal section) reveals a bulging amniotic cavity protruding through the defect in the uterine wall (arrows). Neither peritoneal fluid nor hemoperitoneum was observed. (Reproduced with permission from [11] under the CC Attribution License). The intraoperative finding is presented in Fig. 10.4

CTG is mandatory in patients with clinical suspicion of UR because fetal distress is the most common sign or symptom of UR and frequently precedes any other clinical manifestations of this complication [154].

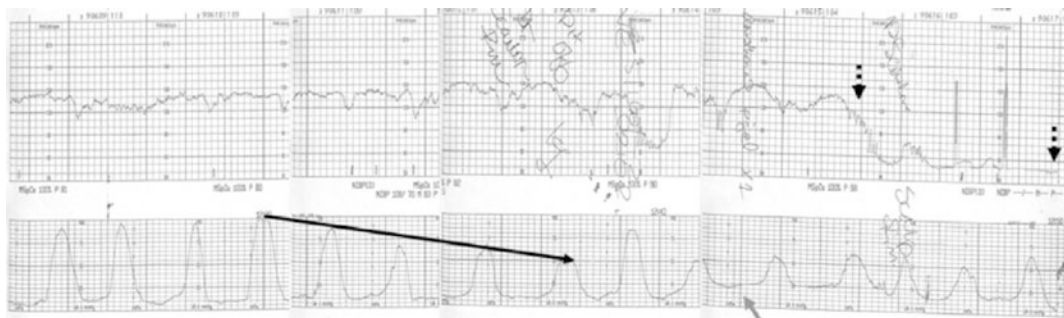
External monitoring (external tocodynamometer) demonstrates the classic sign of complete loss of uterine tone. In contrast, internal monitoring (internal pressure transducer) demonstrates increased uterine resting tone. Both techniques reveal a stepwise gradual decrease in contraction amplitude followed by a sudden onset of profound and prolonged fetal bradycardia in patients with rupture of an unscarred uterus at the term—*staircase sign* (Fig. 10.21). With internal monitoring, the intrauterine pressure catheter does not show a complete loss of resting tone (Fig. 10.22). Internal monitoring has better sensitivity for detecting fetal heart rate and uterine contractions. UR shows the persistence of uterine contractions and increased resting tone, monitored by an intrauterine catheter—findings not observed with external monitoring [12, 182]. However, few



**Fig. 10.21** Uterine contraction pattern during rupture of an unscarred uterus at term. External cardiotocography was used for the tracing. Black arrows show the gradual decrease in the amplitude of uterine contractions (*stair-*

*case sign*). A black arrowhead with a dashed body indicates prolonged fetal bradycardia. (Reproduced with permission from [268])





**Fig. 10.22** Uterine contraction pattern during term rupture of an unscarred uterus. An intrauterine pressure catheter was used for the tracing. The *black arrow* shows the gradual decrease in the amplitude of uterine contractions

(*staircase sign*). *Black arrowheads* with a dashed body indicate prolonged fetal bradycardia. The *gray arrow* shows an increased resting tone. (Reproduced with permission from [268])

papers in the literature documented the type of uterine monitoring used. Furthermore, the uterine contraction pattern may differ depending upon the presence or absence of a uterine scar or the site and direction of rupture. Bradycardia is the most common fetal heart rate abnormality with UR [182, 269]. It may occur due to cord compression within the UR, loss of uterine perfusion, or placental abruption. This staircase pattern appears to be a unique combination of fetal heart rate pattern and uterine contraction pattern that may be of value in diagnosing UR. Fetal bradycardia starts right after or several minutes after the staircase sign [268]. Intermittent fetal heart tone auscultation is mandatory while the patient is off continuous monitoring.

### 10.1.9 Differential Diagnosis

Differential diagnoses in the third trimester and during delivery include placenta previa, placental abruption, uterine atony, and uterine inversion. Moreover, any condition unrelated to pregnancy that may cause hemoperitoneum should be considered in the differential diagnosis. Acute pubic symphysis rupture will be discussed in detail.

#### 10.1.9.1 Acute Pubic Symphysis Rupture

##### Incidence

The incidence of acute pubic symphysis rupture caused by pregnancy varies greatly between

1/600–1/800 [270, 271] and 1/30,000 (older and probably underdiagnosed studies). Risk factors include large fetal birth weight, prolonged labor, epidural anesthesia, nulliparity, shoulder dystocia [272], forceps delivery, and maternal developmental hip dysplasia. Even with these conditions, there is a low risk of a pubic symphysis rupture during or after labor.

##### Pathophysiology

The nonpregnant woman's symphysis pubis gap is 4–5 mm, and it is normal to widen 2–3 mm, without discomfort, during the last trimester of pregnancy. Widening over 10 mm is considered pathologic.

Mechanically, acute pubic symphysis rupture occurs when the fetus descends rapidly into the birth canal during stage 2 of labor, and the head drives into the true pelvis [271]. Despite physiologic laxity during pregnancy, the pelvis cannot adjust quickly enough in rare cases, and the pelvic ring begins to fail at its weakest point—the pubic symphysis.

##### Clinical Presentation

Acute frank pubic symphysis rupture often presents as a sudden onset of severe tearing pain and a sensation of separation directly over the symphysis at delivery or early postpartum. Pain is often immediate and preceded by a “popping” or “snapping” sensation. Other symptoms include tenderness, instability, allodynia, hyperesthesia, or hyperalgesia at and around the joint site. In addition, many women will have difficulty walking. The gait is described as waddling or painful

with the inability to stand or walk. Sometimes, it is possible to hear a clicking sound when the patient walks.

The examination may reveal (1) a palpable gap with edema or hematoma on the soft tissue overlying the symphysis pubis [273, 274], (2) anteroposterior or superoinferior displacement of the upper border of the pubic symphysis or pubic tubercle, or (3) pain during lateral to medial compression of the iliac wings or greater trochanters. One or both SI joints may be tender to palpation. The less acute presentation includes pain, weight-bearing difficulty, and a waddling or wide-based gait. The patient may have a positive *Patrick test*—pain at the sacroiliac joint with flexion, abduction, and external rotation of the hip (with one iliac spine held in a fixed position by the examiner, the woman lies in a supine position, placing her opposite heel on the ipsilateral knee with the leg falling passively outward) [275].

Injuries associated with pubic symphysis rupture include massive bleeding, resulting in hemodynamic instability [276], sacroiliac dislocation [275], sacral fracture, lumbosacral plexopathy [277], and urinary bladder injury.

### Diagnosis

A plain pelvic X-ray is diagnostic. Severe palpatory tenderness of the sacroiliac joint or plain X-ray findings suggests a widening of the sacroiliac joint or sacral fracture. A pelvic CT defines the extent of the injury and posterior ring involvement [275]. According to the clinical presentation, soft tissues are evaluated with MR of the abdomen and pelvis [272].

### Treatment

The first-line treatment is a closed reduction and application of a pelvic binder. Internal surgical fixation is indicated if a gap of the pubic symphysis is >40 mm [272, 277]. Even a gap >40 mm can be treated conservatively, but postpartum pelvic pain persists in most patients [277, 278]. Associated injuries are treated accordingly—sacroiliac joint disruption, vaginal tears, etc. Implants are removed after 6 months [278].

### Prognosis

The prognosis is good to excellent in most cases. All fusions heal, and symptoms improve. Radiographic loosening of implants is observed in subacute cases [279].

## 10.1.10 Treatment

The patient with threatened UR should be examined gently but thoroughly, under anesthesia, by someone experienced enough to carry out whatever treatment method may be indicated. If UR is not diagnosed until after delivery, the procedure depends on the extent of the laceration. The complete UR mandates laparotomy; a cautious plugging from below may be employed in partial UR.

### 10.1.10.1 Anesthetic and Perioperative Management

See Chap. 2.

### 10.1.10.2 Operative Treatment

*The uniformly fatal termination in a very short space of time, of every case of rupture of the uterus that had come to my knowledge in the practice of my friends, or of my own, induced me seriously to reflect what could be done, or what might be rationally attempted, in these deplorable cases*

(William Jackson, 1845 [148])

Around 1845, maternal and fetal mortality was near 100%, and William Jackson (an anatomist and physiologist at the Medical Institution, Sheffield, UK) advocated surgical exploration when UR was suspected [148]. Despite this conclusion, in 1932, Mahfouz still urged conservative treatment whenever possible [280], but today the key to successful treatment is early surgical intervention.

The time available for successful intervention after a frank UR and before the onset of major fetal morbidity is only **10–37 min** from fetal distress on the electronic fetal heart rate monitor [80, 102, 269].



After the fetus is successfully delivered, the type of surgical treatment should depend on the following factors:

- Type of UR,
- Location of UR,
- The extent of UR,
- The degree of bleeding,
- The condition of the mother,
- Future childbearing.

### Suture Repair

Before deciding on the type of surgical management, all rupture locations should be defined. Most URs are at the single site, but anterior and posterior UR (10.7%), bladder, and vaginal involvements (9% and 5%, respectively) are present [43]. Uterine bleeding is more profuse when the uterine tear is longitudinal rather than transverse. “Conservative surgical management” involving uterine suture repair (Figs. 10.23 and 10.24) is reserved for the following findings [149, 250]:

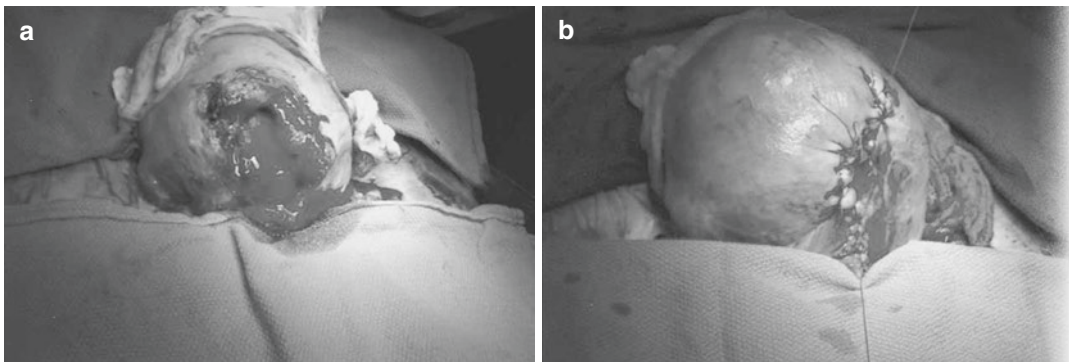
- The desire for future childbearing,
- Low-transverse UR,
- Fundal UR,
- No extension to the broad ligament, cervix, or paracolpos,
- Easily controllable uterine hemorrhage,
- Good general condition,
- No coagulopathy.

Suture repair is not contraindicated in the congenitally malformed uterus [172]. Repair of a UR is achieved in 13–74% of cases [43, 60, 79, 181, 182, 282]. Suture repair carries a recurrence risk of 4–19% in a subsequent pregnancy [14, 283, 284]. Therefore, the women with a previous suture repair of UR should undergo an elective CS when fetal lung maturity is demonstrated [285], or the patient is hospitalized and monitored until 37 weeks. Then CS is performed [286]. Recommendations are not strong because there are no prospective studies.

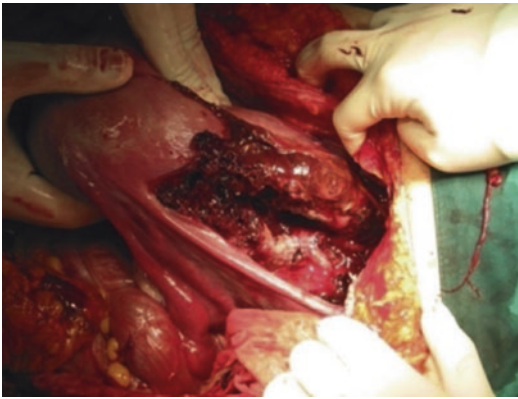
The type and location of UR dictate the type of uterine repair. When the lower anterior uterine wall ruptures, the primary repair is accompanied by hemostatic techniques such as hypogastric artery ligation [149]. The percentage of patients with the simple repair of the uterus is significantly higher in the scarred (90.2%) than in the unscarred uterus group (57.5%). Hysterectomy is performed in 25% of the patients with a previously unscarred uterus, significantly higher than the 9.8% in patients with a scarred uterus [65].

However, if an obvious cause is detected during surgery, and the multiparous woman does not desire future pregnancy, or the future conception may be dangerous, suture repair of the rupture with tubal ligation for sterilization could be performed instead of hysterectomy [287, 288].

In most cases, simple repair of the uterine tear is repaired with a double-layer closure using continuous absorbable sutures [289]. There are cases



**Fig. 10.23** (a) The ruptured and contracted uterus during emergent exploration. (b) The uterine rupture, extending inferiorly from the left side of the previous lower segment scar. (Reproduced with permission from [259])



**Fig. 10.24** Postpartum uterine rupture. The right side of the uterus is ruptured. The right round ligament and uterine artery are intact, making suture repair possible. (Reproduced with permission from [281])

with suture line reinforcement with adhesives (fleece-coated fibrin glue) [77, 290] or patches (Vicryl mesh, Goretex mesh) [291, 292].

### Hysterectomy

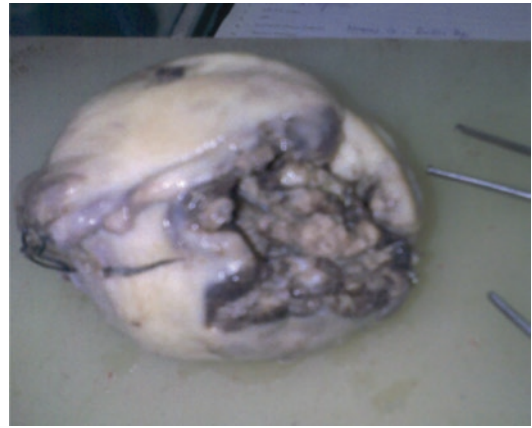
Hysterectomy should be considered the treatment of choice in several indications:

- Intractable uterine bleeding,
- UR sites—multiple, longitudinal, or low lying,
- Placenta percreta,
- Irremediable uterine atony/accrete,
- The probability of cervical cancer,
- Coagulopathy.

The ruptures in unscarred uteri occur most frequently in the corpus uteri and the lateral side and more frequently extend beyond the cervix. These rupture types are surgically more challenging to repair [36].

### Total Abdominal Hysterectomy

Total abdominal hysterectomy is a definitive procedure unless cardiovascular decompensation necessitates subtotal abdominal hysterectomy or simple suture repair with or without bilateral tubal ligation [293]. Previously, total hysterectomy was supported because of the probability of cervical cancer in the cervical stump and the



**Fig. 10.25** Postoperative specimen of the uterus showing large fundal defect after spontaneous uterine rupture of an unscarred uterus due to placenta accreta. (Reproduced with permission from [142] under the CC BY 3.0)

increased rate of bleeding and discharge [294, 295]. The cervical malignancy rate was 0.39–1.9%. Due to cytological surgery, the rate has decreased to 0.1–0.15% [296]. The amount of blood loss, duration of operation, the rate of maternal deaths, ABO need for blood transfusion, and reoperation are higher with total hysterectomy [296].

Placenta percreta is an additional therapeutic issue during spontaneous UR. Up to 1966, there were 33 cases published [297], and in the period from 1966 to 2000, another 40 cases were published [298]. Spontaneous UR due to placenta percreta (Fig. 10.25), with partial manual removal and hysterectomy, has 20% mortality. During hysterectomy with no attempt at manual removal results in 100% survival. When the adherent placenta was left in situ, 67% succumbed.

The treatment of choice for the UR with placenta percreta is a total abdominal hysterectomy with no attempt at manual removal [297, 299, 300].

The *fundal hiatus* discovered in a presumably unscarred uterus at emergency CS for other obstetric indications, with the appearance of the fibrotic edge of the defect, strongly suggested a chronic event (rupture or previous perforation) with the possible expulsion of the previous conception. A

hysterectomy is recommended. If the defect is sutured, an intraoperative or definitive biopsy of the edges of the defect is mandatory [301].

### Subtotal Hysterectomy

Subtotal hysterectomy is preferred with the shorter operation to minimize mortality and morbidity, as in [296]:

- Hemodynamic instability,
- Cardiovascular decompensation.

These recommendations are for emergency hysterectomies, not only spontaneous URs representing 10% of cases [296]. Total abdominal hysterectomy for spontaneous UR is done in 14%, subtotal hysterectomy in 5–22%, uterine repair with bilateral tubal ligation in 25–45%, and uterine repair without bilateral tubal ligation in 39% of patients [20, 41].

While performing a subtotal hysterectomy following the dehiscence of a lower segment scar, the incision may be posterior and circumferentially from the rupture [22]. In such cases, total hysterectomy carries the risk of ureteric injury. During the operation, the placenta should be examined and evacuated. It can be found in the abdominal cavity or placed intrauterine. The amniotic sac can be intact (Fig. 10.26) [250, 302] or disrupted.

The extent of endometrial activity within the horn and the degree of separation to the other side influence management. However, these factors are not included in any formal classification. If the rupture is due to rudimentary horn pregnancy, separating the placenta from the rudimentary horn is difficult or impossible. In such cases, the rudimentary horn of the uterus, along with the placenta, should be excised (see Chap. 9) [303] or a subtotal hysterectomy performed.

### First and Second Trimester

Case reports of UR management in the first or second trimester are limited [149, 150, 195, 287, 304, 305]. Often, the clinical condition of the patients requires an emergency hysterectomy. The most important issues are whether the UR repair can withhold the tension from the enlarging uterus



**Fig. 10.26** Intraoperative photograph shows the uterus (lower part of the operative field), the gestational sac (on the left), and the placenta (upper right) after opening the abdomen. (Reproduced with permission from [302] under the CC Attribution License)

and significant forces developed during labor. However, there have been reports of the conservation of the uterus. A midgestational UR, repaired using fibrin-coated collagen fleece, allowed the successful continuation of the pregnancy [290].

### Urinary Bladder Rupture or Injury

See Sect. 28.3.

### Elective Cesarean Section

A recurrent UR rate of 4–29% has been noted in patients with a prior repair [60, 85, 245, 306, 307], although a simple repair of a UR can result in no cases of recurrent UR [308].

A patient with a previous UR can carry another pregnancy. The woman with a previous UR should undergo an elective CS as soon as fetal lung maturity can be demonstrated [66, 282, 285, 309]. CS between 37 and 38 weeks is recommended for patients with a previous ruptured lower uterine scar. For those with a history of ruptured classical scar or previous UR, the opinion varies regarding delivery time. Some deliver at 35 weeks, while others recommend admission to the hospital 1 week before the gestational age at which labor started in the previous pregnancy [85].

### 10.1.11 Prognosis

*The fatality of this dreadful accident to the parturient female demands our sympathy, and calls for our utmost exertions to devise some means of relief, if any can be found, under the circumstances presenting an almost hopeless condition of our patient; for an escape from this terrible disaster may be considered almost miraculous.*

(William Jackson, 1845 [148])

*Rupture of the uterus is one of the most dangerous accidents to which the female in the puerperal state is liable: and one from which recovery is hardly to be expected, either of the mother or the child.*

(Ames RPM, 1881 [5])

Maternal and perinatal mortality vary significantly between developed and developing countries. Also, these rates are highly variable in the same country, especially between cities and rural areas. Due to the rarity of the disease and improvement in diagnostic and therapeutic modalities, mortality is decade-dependent and is continuously decreasing.

#### 10.1.11.1 Maternal Outcome

##### Repeated Uterine Rupture

In the 1930s, after a simple suture of the tear, several cases in a subsequent pregnancy resulted in a repeated UR [284, 310]. It is difficult to estimate the risk of repeated UR due to (1) a high frequency of hysterectomy, (2) pregnancy avoidance after explaining possible similar risks in further pregnancy, or (3) tubal ligation performed during UR repair. The women with UR after TOL have a lower risk for another UR than women with previous UR during pregnancy. With a history of UR, the recurrence rate ranges from 0% to 33%, which recently decreased to 4–15% [311].

##### Maternal Morbidity

The maternal morbidity rate ranges from 12% to 46% [15, 248, 312]. Commonly reported maternal morbidity includes hemorrhage and shock, overall 46%; infection (wound infection, 13.8%; peritonitis, 10.2%; tubo-ovarian abscess or urinary tract infection, 19.8%; pelvic inflammatory disease, 4.3%; respiratory infections including pneumonia, 2.2%; and tetanus, 2%); vesicovagi-

nal fistula, 6.6%; pelvic hematoma (mostly in the broad ligament), 19.2%; fever, 21.7%; and paralytic ileus, 18.9%.

Surgical complications include injury to the bladder and ureter [22], dehiscence, and hernia. Less commonly, hematuria, renal failure, disseminated intravascular coagulation, atelectasis, thrombophlebitis, pulmonary and cerebral embolism, and intestinal obstruction are reported. Up to 58% with UR required  $\geq 5$  units of blood [79].

A hysterectomy rate varies from 6% to 83% [60, 79, 80, 102, 168, 181, 182, 282, 313]. In a study with a hysterectomy rate of 19%, 68% were performed because the uterus was not deemed repairable, 21% for irremediable uterine atony, and 5% because of placenta accreta [80]. URs outside the lower segment are negatively associated with healthy mothers [36]. A significantly higher rate of hysterectomy was (1) before 1980, (2) with an unscarred uterus, (3) parity  $>3$ , (4) postpartum after vaginal delivery, and (5) URs outside the lower segment (most URs occurred outside the lower uterine segment in unscarred uteri (79.3%)) [36, 314]. The hysterectomy rate from complete UR is 21–26% [24, 36, 314].

The increased morbidity in women with unscarred uteri may be due to the increased vascularity at the rupture site and a tendency among providers to delay treatment due to the low index of suspicion in the absence of an operative uterine history [36].

##### Maternal Mortality

Maternal mortality depends on the following:

- Cause,
- Decade of presentation,
- Country development,
- Type and extension of the uterine tear,
- Treatment delay.

Maternal mortality until 1881 was 88%, and 90% of deaths occurred within the first 10–15 min of the onset of symptoms [5]. In 1966, 29% (2/7) of patients who underwent repair of a UR later



presented with another UR in a subsequent pregnancy, and one of these women died [245]. Maternal mortality in general occurs at a rate of 0–1% in developed countries [36, 119, 315], but in developing countries at the rate of 2–11% [20, 25, 27, 45, 293, 316, 317] and even 30% reported in Nigeria [43, 47, 318]. UR is an important cause of maternal mortality in less and less developed countries, accounting for 9.3% of maternal deaths [319]. In the Second Report on Confidential Enquiries into Maternal Deaths in South Africa 1999–2001, UR caused 6.2% of deaths due to direct causes and 3.7% of all deaths (1.9% due to rupture of an unscarred uterus and 1.8% due to rupture of a scarred uterus) [320, 321]. UR was the only cause other than sepsis to have increased since the previous report, possibly due to the widespread use of misoprostol in uncontrolled dosages for labor induction [73, 322, 323].

In a South African study from 1976, with a mortality rate of 8.5% due to the rupture of an unscarred uterus, deaths could be subdivided into mortality for women with longitudinal uterine tears (8.2%), transverse tears (4%), posterior wall tears (13%), and multiple uterine tears (25%). Golan et al. reported no deaths among 32 mothers who experienced a rupture of a scarred uterus compared with 15% of women with an intact uterus [60]. The maternal mortality rate associated with UR largely depends on whether the diagnosis is established before (4.5%) or after delivery (10.4%) [313]. The incidence of twin pregnancy is 5% of rudimentary horn pregnancies, and the overall survival rate is 2.4% [315]. The mortality associated with hysterectomy was higher than for suture repair. Patients with more extensive, multiple, or infected tears were unsuitable for repair and tended to be much more acutely ill, contributing to the high mortality rate [43, 72].

### 10.1.11.2 Fetal Outcome

#### Fetal Morbidity

Significant neonatal morbidity occurs in women with UR when more than 10–37 min elapses between the onset of prolonged decelerations and successful CS [80, 102, 269]. Many decades ago, it was 29%, mainly causing nervous system dam-

age or pulmonary disease [146]. Most surviving mothers had a mean blood loss of more than 2000 mL [149, 165]. Maternal hemorrhagic shock is a risk factor for fetal mortality and morbidity.

#### Fetal Hypoxia

Leung et al. found that 5% of neonates born to women with URs developed neonatal asphyxia (defined as umbilical artery pH <7 with seizures and multiorgan dysfunction). No clinically significant perinatal morbidity is present when the delivery is accomplished within 17 min of an isolated and prolonged fetal heart rate deceleration. If severe, late decelerations preceded prolonged deceleration, perinatal asphyxia is observed at 10 min from the onset of the prolonged deceleration to delivery [80]. Also, 55% of fetuses born after UR had bradycardias between 18 and 37 min before delivery. Although the rate of fetal acidosis was high (91%), no permanent neurological injuries or neonatal deaths occurred [269]. Even with rapid (<18 min) intervention between prolonged fetal heart rate deceleration and delivery, 5–10% of neonates developed hypoxic–ischemic encephalopathies with impaired motor development [88, 121]. Although the rapid intervention did not always prevent severe metabolic acidosis and severe neonatal disease, it probably did limit neonatal death.

In 99 cases of UR, 43% had an umbilical artery pH <7, and 58% of these newborns had a pH <6.8. Regarding these pH levels, 39% had 5-min Apgar scores of <7, and 12% had 5-min Apgar scores of <3 [80]. Around 91% born after UR had an umbilical artery cord pH level <7.0, and 45% had 5-min Apgar scores <7 [269].

The most important factor for the development of fetal acidosis is the complete extrusion of the fetus and placenta into the maternal abdomen [269].

#### Hypoxic–Ischemic Encephalopathy

Descriptive neonatal consequences (fetal acidosis, Apgar scores, need for resuscitation, and



intensive care unit admissions) are poor predictors of neonatal morbidity. UR is associated with a significant increase in the risk of neonatal encephalopathy compared with a nonreassuring fetal status [324]. UR can result in acute and profound asphyxia, which might explain the predominant basal ganglia and thalamic injury pattern observed in newborn babies [325, 326]. One-third of delivered infants after a UR showed hypoxic–ischemic encephalopathy, and in 19%, it was moderate or severe [324]. The prevalence of hypoxic–ischemic encephalopathy is expected to increase due to decreased fetal mortality. However, hypoxic–ischemic encephalopathy is rare, and most recover without sequelae [37].

Fetal Mortality

The highest risk of intrapartum/infant death was when UR is associated with placental separation or fetal extrusion [37, 80, 327], regardless of time to delivery [37, 327].

Up to the year 1848, almost all fetuses died. One-day survival of delivered fetuses was 37%, but mortality of the survived fetuses after 24 h was 46% [3]. The initial mortality of undelivered fetuses was 23%. Mortality after 24 h was 73% [3]. Fetal mortality is highly variable. The most developed countries have a fetal mortality rate of 4.7–26.2% [37, 62, 66, 327, 328]; less developed countries claim 54.3–81.7% [15, 25, 27, 41, 293, 316], with up to 91–93% in Pakistan, Uganda, and Nigeria [20, 40, 43, 44]. Risk factors for fetal mortality are presented in Table 10.3.

The decade of analysis is prognostic. The complete UR with infant death in Norway was present in 51.6% during 1967–1977, while dropped to 15.0% from 2000 to 2008 [37].

Older studies claimed two to three times lower fetal mortality in the scarred UR group [65, 146], although newer studies did not find a difference [37]. The explanation is that many unscarred URs are detected postpartum, indicating that UR occurred shortly before delivery, with a short duration of hypoxia [37]. The UR was three times more likely to result in the death of the infant if the

**Table 10.3** Risk factors for fetal mortality from complete UR are [37, 65]

| Obstetric                  | Maternal          | Other                                     |
|----------------------------|-------------------|-------------------------------------------|
| Unscarred uterus?          | Parity ≥3         | Decade                                    |
| Sudden loss of contraction | Hemorrhagic shock | The time from rupture to delivery >30 min |
| Placental separation       |                   | Delivery after midnight                   |
| Infant extrusion           |                   | Occurrence outside the hospital           |

delivery took place in a hospital with <3000 births a year (1/1300) compared to hospitals with >3000 births a year (1/4700) [329]. The differences exist if preterm infants and different populations are included (all women in labor vs. women undergoing a trial of labor after a previous CS) [88].

Time intervals <20 min had the least intrapartum/infant deaths. For every additional minute, there was a 10% increase in intrapartum/infant deaths and a 5% decrease in delivering a healthy infant [37].

Between 1990 and 2000, newborn survivors’ average gestational age and weight were 32 weeks and 1770 g, respectively [315]. Fetal mortality after UR with the previous salpingectomy as a possible cause is 67% [238].

There are no comparisons of the type and the location of UR and fetal mortality and morbidity. In six cases of posterior UR after the previous CS, in only the last case, both mother and fetus survived [33]. Scars outside the lower segment were associated with a higher percentage of catastrophic prelabor UR than scars in the lower segment, resulting in a high perinatal death rate [37].

There are cases of delivery of a live fetus from abdominal pregnancy due to unrecognized UR [330, 331].

10.2 Traumatic Uterine Rupture

10.2.1 Historical Perspective

For a historical perspective of spontaneous UR, see Sect. 10.1.1. First, Baisch then De Lee [332] divided URs into spontaneous and traumatic. Lazard and Kliman, in 1936, proposed a classification of trau-

matic URs [333]. Traumatic URs are due to criminal abortion (better termed “instrumental” trauma) or a result of blunt abdominal trauma, complicating about 0.6% of traumas during pregnancy [334].

The first two cases are from 1706 and 1709, resulting from a fall at the sixth and seventh months of gestation. One fetus was expelled through the anus and another through the navel [335, 336]. Joseph. B. De Lee, in 1904, described the eighth month pregnant woman falling through a broken stair, the body falling till the protuberant abdomen was arrested by the narrow opening. Complete UR was at the fundus resulting in fetal death [332]. Cases by Ley in 1919 and Hosking in 1923 followed. The first cases of fetal death due to traumatic UR from MVA were by Woodhull in 1942 [337] and Elias (boat collision) in 1950 [338].

### 10.2.2 Incidence

Up to and including 1929, Estor and Pueck (referred to by Jaroschka, Medizinische Klinik, 1929) collected 40 cases. Additional cases in the 1930s were collected by Orthner [339], Lazard and Kliman [333], and Ruder and Moore [340]. During the last 50 years, motor vehicle use increased blunt abdominal trauma resulting in traumatic UR [341–343]. Over 100 cases of traumatic rupture of the pregnant uterus have been reported until 1975, with only three [338, 344, 345] with the avulsion of the uterus. The overall incidence of all-cause UR significantly varies. In patients hospitalized for assault during pregnancy, the incidence of UR reached 0.71%, with an odds ratio of 46 compared with women with no history of assault [346]. Traumatic placental abruption is the most common injury after blunt maternal abdominal trauma, and traumatic UR in the 1980s was present in 10% of cases [347].

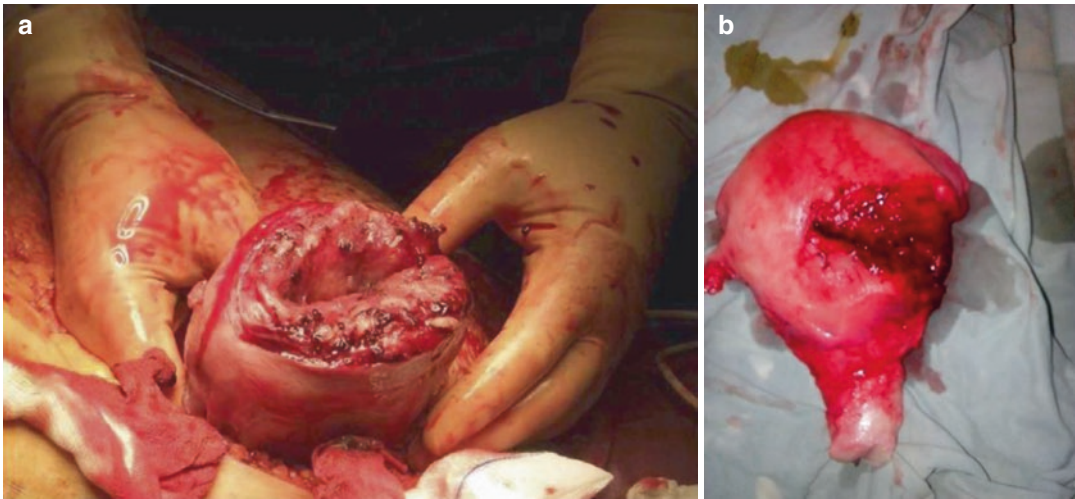
### 10.2.3 Etiopathogenesis

See Sect. 25.3.3.3. While a trauma of sufficient force may cause a rupture in a healthy uterus, the presence of a weakened point caused by preceding disease, such as hyaline degeneration of mus-

cle fibers resulting from multiparity, previous curettages, placenta previa, intramural fibroids, etc., would undoubtedly increase the probability of UR resulting from external violence. Orthner gives the following explanation of the mechanics of the injury [339]: as to whether the blow or the resultant fall is the principal factor, one can assume that whichever is of the greater intensity is the chief factor, i.e., with a slight blow and a fall from a great height, the latter is the main factor; with a severe blow and a shortfall to the floor, the blow in all probability is to blame. It is not possible, as a rule, to determine the kind and direction of the force from the location of the UR, as this usually occurs by counter-coup.

The rupture is always the result of a sudden increase in the intrauterine pressure caused by the sudden compression of the abdominal contents. By the laws of hydrodynamics, this pressure spreads equally in all directions in the uterine cavity filled with amniotic fluid. The tear occurs at the weakest point of the uterine wall. At the end of pregnancy, the point is at the fundus [333], which lacks the protection of the bony pelvis. In many cases, the placental site is especially weak because of the increased vascularity. It is unknown whether uterine scar from previous CS indicated due to myomectomies is prone to rupture. The rupture site directly relates to the site where direct traumatic or counter-coup forces are applied, mainly involving the uterine fundus (Fig. 10.27a). However, other locations and degrees of UR from other causes have been reported (Fig. 10.27b) [334, 349–351]. This is because amniotic fluid transmits high pressures efficiently; “blast injuries” can follow blunt trauma, resulting in rupture of the uterine fundus in 75% of cases. During the first trimester, the pelvis protects the uterus, and uterine avulsion can likely occur solely in combination with a pelvic ring fracture [345]. Even cases with the seatbelt as the proposed etiologic factor exist [352].

The extent of the UR can be variable. Such an injury may result in serosal hemorrhage or abrasions, avulsion of the uterine vasculature with bleeding, complete disruption of the myometrial wall with extrusion of the fetus, placenta, or

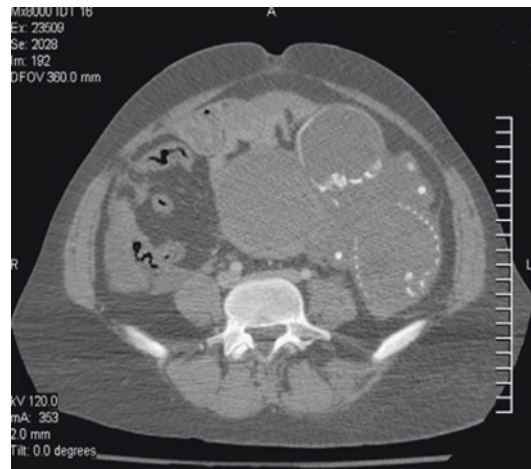


**Fig. 10.27** Ruptured uterus. (a) The most common location is the uterine fundus [348], but other locations (b) can rupture depending on the mechanism of trauma. (Reproduced with permission from [349] under the CC Attribution License)

umbilical cord into the abdominal cavity; or complete uterine avulsion [353].

#### 10.2.4 Clinical Presentation

The seatbelt sign is a strong predictor of traumatic UR [350, 354]. Clinical presentation varies from subtle findings (e.g., uterine tenderness, nonreassuring fetal heart rate patterns) to a rapid onset of maternal hypovolemic shock. The classic description of UR includes the following: severe uterine pain and tenderness, profound shock, palpation of fetal parts outside the uterus, and vaginal bleeding. The examination can reveal a (moderately) distended abdomen with suprapubic tenderness and guarding. The uterus can be difficult to palpate. Pelvic examination confirms normal external genitalia and closed firm cervix. Fullness in the pouch of Douglas can be found with the examining finger stained with blood. The presence of maternal hypotension is a late and ominous sign. These complex findings, however, often are not present [15, 355, 356]. Consequently, the diagnosis is often delayed or not considered at all. The hemodynamic stability of the mother is maintained at the expense of uterine blood flow, putting the fetus at risk [357, 358]. Consequently, fetal distress may be the first indicator of unsuspected maternal hemorrhage.



**Fig. 10.28** Abdominal CT shows the fetus in the abdominal cavity and hemoperitoneum, findings consistent with complete uterine rupture [348]

#### 10.2.5 Diagnosis

The diagnostic modalities used depend on the severity of the maternal injury. The fetus can be palpated in the abdomen outside the uterus in severe abdominal trauma with UR. Alternatively, abdominal CT can confirm this condition (Fig. 10.28). On plain (abdominal) X-rays, the fetus can be found in abnormal positions, such as in the mother's thigh (Fig. 10.29).



**Fig. 10.29** The fetus was found lying just under the skin and superficial fat on the upper anterior surface of the right thigh. (Reproduced with permission from [359])

Coutts explained two possible mechanisms [359]:

1. The bus struck the woman on her left side, throwing her on the ground, and went over her; the pressure of the tires and counterpressure of the ground ruptured the uterus, and the pressure continuing downward and to the right forced the fetus down into the thigh (the fetus was about 23 weeks old, so the uterus would be above the brim and nearing the level of the umbilicus),
2. The original blow and pressure were on the right side and stripped the skin and superficial fascia of the thigh, detaching the inguinal ligament from its attachments and the abdominal muscles from the anterior third of the iliac crest; the same force continued to act, tore the peritoneum, and ruptured the uterus. On the release of the pressure, the uterus rebounded forward and squeezed out the fetus, which

**Table 10.4** (Pregnant) uterus injury scale

| Grade <sup>a</sup> | Description of injury                                                     | AIS-90 |
|--------------------|---------------------------------------------------------------------------|--------|
| I                  | Contusion or hematoma (without placental abruption)                       | 2      |
| II                 | Superficial laceration (<1 cm) or partial placental abruption <25%        | 3      |
| III                | Deep laceration (≥1 cm) in second trimester or placental abruption 25–50% | 3      |
|                    | Deep laceration (≥1 cm) in third trimester                                | 4      |
| IV                 | Laceration involving uterine artery                                       | 4      |
|                    | Deep laceration (≥1 cm) with >50% placental abruption                     | 4      |
| V                  | Uterine rupture                                                           |        |
|                    | • Second trimester                                                        | 4      |
|                    | • Third trimester                                                         | 5      |
|                    | Complete placental abruption                                              | 4–5    |

Reproduced with permission from [360]

<sup>a</sup> Advance one grade for multiple injuries up to grade III

passed out under the skin of the right thigh along the line of least resistance.

10.2.6 Treatment

The diagnosis of UR warrants immediate obstetric intervention. As to therapeutic procedure, much depends on the location of the rupture and the degree of injury (Table 10.4).

Total abdominal hysterectomy is considered the operative intervention of choice, although subtotal hysterectomy or simple suture repair may be reasonable alternatives [15, 356]. If it occurs in the fundus, a laceration repair is quick and is done with less shock. If the tear is in the lower segment, transverse hysterectomy is indicated. Palliative measures must be considered and might be lifesaving, such as applying the Momberg belt or clamping the uterine arteries through the cervix until the patient can be relieved of shock and prepared for surgery.

10.2.7 Prognosis

UR tends to occur only in the most severe accidents involving direct abdominal trauma. This event can be catastrophic for both the mother and

her unborn fetus, especially when there is a delay in the diagnosis since initial symptoms may be variable. With traumatic UR, fetal mortality approaches 100% and maternal mortality is close to 10%, with most maternal deaths due to concurrent injuries [334, 361, 362]. Maternal survival results from blood vessel constriction when the bleeding rapidly diminishes or even stops. The uterine contents (the placenta, the amniotic sac, etc.) are immediately emptied into the abdominal cavity. After that, the uterus contracts as it would following CS. Since the blood supply at the midline (where the rupture usually occurs) is scanty, the uterine muscle contractions practically stop the bleeding. This suggests that when the placenta is inserted more toward the parametrial region, with lower contractibility and larger blood vessels, the trauma will result in fatal exsanguination.

More than 50% require  $\geq 5$  units of blood after UR, and hysterectomy rates are 26–83% [342].

## 10.3 Uterine Perforation

### 10.3.1 Traumatic

See Sect. 25.4.

### 10.3.2 Iatrogenic

#### 10.3.2.1 Incidence

Uterine injury or perforation can be from serosa-to-mucosa or mucosa to serosa. Serosa-to-mucosa injury occurs during open [363] or laparoscopic [364–367] procedures. Mucosa to serosa injury occurs during instrumental transvaginal procedures, like curettage (see Sect. 18.3). The most common emergent surgical operations during pregnancy are appendectomy and cholecystectomy. Therefore, iatrogenic uterine injuries most commonly occur during these procedures, mainly by laparoscopic access from a blind Veress needle or trocar insertion [363–367]. Due to the similarity with fetoscopy, this inadvertent uterine perforation is termed *incidental fetoscopy* [366].

#### 10.3.2.2 Pathophysiology and Presentation

Incision or perforation through the full thickness of the uterine wall can lead to the following complications: (1) bleeding from the incision site, (2) leakage of amniotic fluid, (3) the contamination of amniotic fluid with the purulent or feculent material, (4) CO<sub>2</sub> insufflation into uterine wall or intrauterine cavity [368, 369], which can lead CO<sub>2</sub> embolism, and (5) pneumoamnion [367].

Most cases are discovered during the initial operation.

#### 10.3.2.3 Diagnosis and Treatment

The knowledge about this issue arises from the operative fetoscopy. It involves inserting a 1.2- to 3-mm trocar under US guidance through the maternal abdomen and uterus into the amniotic cavity to access the fetus, placenta, or umbilical cord. After the procedure is completed, the trocar(s) are removed from the abdomen. The sites of uterine perforation from the trocars generally do not require repair [366].

Accidental perforation of the pregnant uterus during laparoscopy necessitates intraoperative obstetric consultation. Conversion to laparotomy is unnecessary if adequate inspection and potential repair of the uterus can be obtained by laparoscopy. When the uterine injury is recognized during the operation, first, the operator should verify whether the amniotic sac is intact. The US should be performed to determine a fetal heart rate and residual amniotic fluid volume [366]. The gestation could continue with a live fetus and enough amniotic fluid and no significant bleeding. If the defect is minimal, from a Veress needle or 5 mm trocar puncture, there is no indication to suture the defect [368]. Larger lacerations should be repaired with 2-0 absorbable sutures in a single layer [366]. Additional suturing could potentially cause more harm by increasing the risk of membrane rupture. If significant leakage occurs or there is a dilemma about fetal vitality, the baby should be delivered by CS during the same operation. If the advanced gestation continues with a viable fetus, postoperative corticosteroids should be considered due to the risk of preterm labor [366]. Fetal middle cerebral artery Doppler

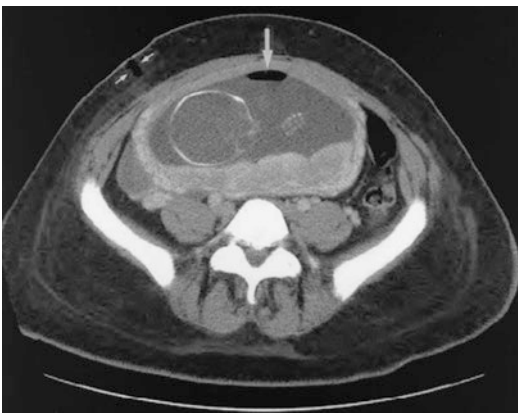


assessment evaluates fetal anemia, especially when placental perforation is suspected. Anti-D immunoglobulin should be administered to any Rh-negative patient, and a Kleihauer-Betke test should be obtained [366]. Before hospital discharge, fetal and amniotic fluid status should be checked with US [366].

CO<sub>2</sub> embolism should be suspected when maternal hypotension occurs after CO<sub>2</sub> insufflation through the Veress needle [369]. In the early postpartum surgery, or after the termination of pregnancy, the Veress needle insertion into the uterine cavity results in the gas escaping through the cervical os [369].

The use of perioperative broad-spectrum antibiotics prevents the risk of chorioamnionitis. WBC and CRP should be measured once or twice daily to detect chorioamnionitis early. Cardiotocography should be performed daily. The immediate risk of preterm labor is addressed by using indomethacin (see Chap. 4). However, a calcium channel blocker is also an option and would not affect the amniotic fluid volume or potentially mask an infection.

If the injury is unrecognized during the operation, pneumoamnion causes increasing maternal abdominal pain. An abdominal CT shows pneumoamnion (Fig. 10.30).



**Fig. 10.30** Postoperative abdominal CT shows an air-fluid level (pneumoamnion) within the amniotic cavity (large arrow) and subcutaneous air from the laparoscopic trocar insertion site (small arrows). (Reproduced with permission from [364])

### 10.3.2.4 Prognosis

The risks of operative fetoscopy include PPROM, oligohydramnios, preterm delivery, chorioamnionitis, fetal injury, and pregnancy loss. Additionally, there are concerns about the potential risk of fetal anemia, placental abruption, and fetomaternal hemorrhage when the trocar perforates the placenta [370]. However, some studies did not find significant differences in rates of PPROM, placental abruption, miscarriage, or perinatal survival [371].

Despite the rarity of publications on the subject, similar complications and outcomes can be expected for operative fetoscopy. There is an increased rate of preterm labor after iatrogenic uterine injuries [366]. Although some recommend CS before the onset of labor to minimize the risk of spontaneous UR [372], small defects that were not sutured during the initial operation heal without evidence of prior uterine injury [366]. Therefore, with small punctures, vaginal delivery should be preferred. A single case of pneumoamnion resulted in the spontaneous rupture of membranes with the delivery of a stillborn [367].

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## Abstract

Torsion of the gravid uterus, a frequent disorder in veterinary obstetrics, is extremely rare in humans but is more common than torsion of a nongravid uterus. Physiological dextro-rotation is common in pregnancy. If additional risk factors for uterine torsion are present, such as uterine anomalies, myomas, or fetal disproportions, uterine torsion has a higher incidence of occurrence. The clinical presentation of uterine torsion is variable and nonspecific. Symptoms depend on the degree of torsion, the speed at which the torsion develops, duration of torsion, and stage of pregnancy, labor, or puerperium. Differential diagnosis is almost always obstetric, mostly spontaneous uterine rupture or obstructed labor. The diagnosis should be made promptly for two reasons: (1) to save the fetus and (2) to prevent ischemic uterine changes, which could lead to uterine necrosis, indicating hysterectomy. Before irreversible uterine ischemic changes occur, early intervention enables uterus preservation with the possibility of normal future pregnancies. Detorsion is a method of choice. If not successful, hysterotomy with Cesarean delivery helps in uterine detorsion.

## 11.1 Historical Perspective

*No tumor, no torsion.*

(J. Barozzi, 1907 [1])

*No uterine abnormality, no torsion.*

(Leyland A. Robinson and  
Muriel H. Duvall, 1931 [2])

The earliest report of uterine torsion (UT) in pregnancy was made by an Italian veterinarian, Hippiaper Columbi, in 1662 [3] because gravid UT is more common in animals (cattle). Almost 200 years later, in 1863, Virchow reported the first case of the nongravid UT in a human at postmortem examination [4]. Léon Labbé (1832–1916), a French surgeon from Paris, first described this abnormality with maternal survival in 1876 and then Leopold Reinprecht in Germany in 1899 [5].

## 11.2 Incidence

Uterine torsion is the rotation of the uterus on its longitudinal axis  $\geq 45^\circ$ .

Gravid UT, a frequent disorder in veterinary obstetrics, is extremely rare in humans [6–8] but is more common than nongravid UT. During the

long period between 1876 and 1992, there were 212 cases [9]. Between 1996 and 2006, Wilson et al. found another 38 cases [10]. Between 2006 and 2020, 41 gravid UT have been reported [11]. Therefore, 300 cases have been published in the last 150 years.

Most UT is detected in the third trimester [10, 11]. The earliest reported period for UT during pregnancy is in the sixth gestational week; the latest is in the 43rd week. Most UTs diagnosed at term are during the first stage of labor. Only six cases of puerperal UT exist [12–14].

### 11.3 Etiopathogenesis

In its normal state, the uterus has little mobility and is firmly held by the broad and uterosacral ligaments. These widely distributed supports resist any tendency to UT. The uterus becomes an abdominal organ during pregnancy with exaggerated congenital and physiological rotations and obliquities of the normal uterus. During pregnancy, a relatively small increase in the length of the broad ligaments causes the uterus to curve around the attachment point. This anatomical arrangement permits increased uterine mobility in late gestation with a predisposition to UT. An additional factor is an elongated cervix with structural weakness and angulation in the isthmic region leading to UT. The structural weakness may be developmental or acquired [15].

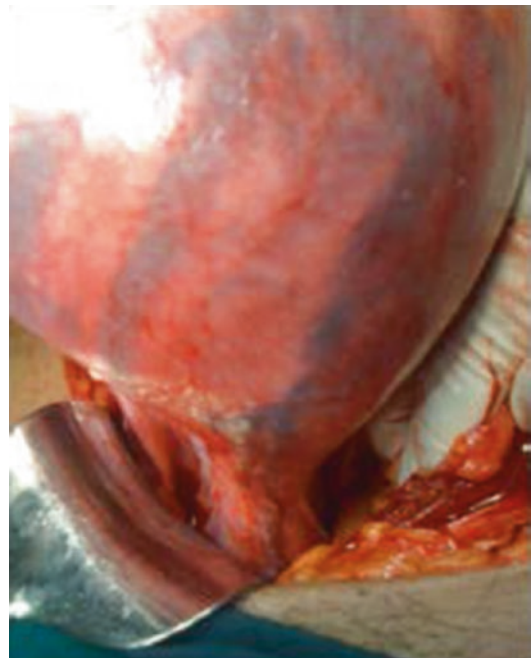
Physiological dextrorotation occurs commonly in pregnancy with a normal orientation of the myometrium fibers. Approximately 80% include dextrorotation, while levorotation is present in 20% [16]. A degree of more than 30° is considered pathological during pregnancy, but it is insufficient to obstruct the normal uterus' blood supply [17]. Further rotation will give rise to symptoms depending on the degree of UT, the stage of pregnancy, and the speed at which the UT develops [18].

In most cases, the degree of torsion is 180° [16]. Since 1985, only 46 cases during pregnancy were published, and none with a rotation of  $\geq 270^\circ$  [19]. However, there were cases with the rotation of 540° [20, 21] and even 720° [22],

which results first in venous engorgement (Fig. 11.1), and then, when arterial blood supply is arrested, in uterine necrosis [16, 24].

#### 11.3.1 General Population

The presence of a uterine tumor was believed to be the main etiological factor in the development of UT, and in 1907, Barozzi made the statement “no tumor, no torsion” [1]. Leyland A. Robinson and Muriel H. Duvall, in 1931, modified that statement to “no uterine abnormality, no torsion,” and they presented the hypothesis that uterine rotation in the absence of gross disease was due to a developmental asymmetry of the myometrium [2]. Uterine anomalies occur in 0.1–0.5% of all women [25, 26]. The most common are symmetric or duplication anomalies, including didelphic, bicornuate, and septate uteri. Bicornuate and septate uteri occur more frequently than didelphic uteri. In malformed uteri, the discrepancy in uterine vascularity and the



**Fig. 11.1** Untwisted 180° levorotated gravid uterus with venous engorgement. (Reproduced with permission from [23])

development of one-sided muscular and fibrous attachments cause the pregnant horn to develop a high degree of mobility. Even abdominal trauma during pregnancy can be the cause [27]. For example, a large, heavy fibroid of the subperitoneal type attached near the fundus of the uterus and well above the pelvic brim may rotate and exert traction on the uterus. It has inertia and a wide field of movement, and the more spherical its shape, the more easily it can rotate. Sessile leiomyoma increases the risk of UT [28].

However, as early as 1935, Reis and Chaloupka found UT unassociated with any uterine abnormalities during normal pregnancy and within a typical pelvis [19, 29]. In approximately 20%, no causative factor is apparent [28], although a common feature in many cases has been a previous cesarean section (CS). MRI studies proved that defective isthmic healing after lower uterine segment CS might result in suboptimal restoration of normal cervical length [27, 30]. This may result in an elongated cervix with structural weakness and angulation in the isthmic region and may predispose to UT. Sometimes intrinsic pelvic pathology is the cause.

### 11.3.2 Pregnancy

The common risk factors reported in association with UT are often nonspecific. Changes due to pregnancy play an important role, but the phenomenon is more common in nulliparous women, while maternal age and parity seem to play no part in UT [9, 31]. In 1931, intrinsic intrapelvic pathology was responsible for 66% of UT during pregnancy [2], and a kyphotic pelvis was an occasional cause of gravid UT [32]. According to Piot et al., 31.8% had uterine myomas, 14.9% had uterine anomalies, especially the bicornuate uterus, 8.4% had pelvic adhesions, 7% had ovarian cysts, 4.6% had an abnormal presentation and fetal anomalies, 2.8% had abnormalities of spine and pelvis, and no discoverable causes in the rest of the cases were found [16]. Since 2006, 10% were twin pregnancies [33].

With sudden falls, sudden pushes from other people, and bumpy movements during transpor-

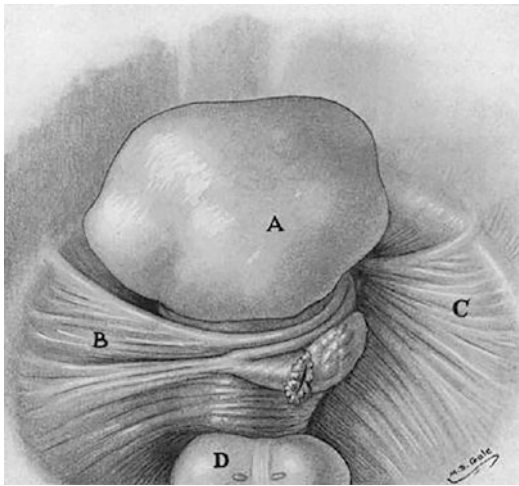
tation, the fetus in the advanced pregnant uterus may respond with violent movements exposing the unstable pregnant uterus to torsion. Contractions of the abdominal muscles or the degree of filling of the bladder and distension of the intestines could contribute. Possibly excessively lax abdominal wall muscles allow UT to occur [34, 35]. A reduced amount of amniotic fluid decreases the distance between a fetus and the uterine wall. The fetus feels abrupt movements of the dam as a painful stimulus and, in response, performs strong reflexive movements that may cause the rotation of the uterus. A reduced amount of amniotic fluid also decreases the size of the uterus, allowing free intra-abdominal uterine movements. The twisting of the uterus puts pressure on the middle uterine vein, which results in disturbances in the venous circulation and increases the CO<sub>2</sub> tension in fetal blood. As a result, the fetus makes vigorous movements, which aggravates the condition and causes the uterus to be turned to a higher degree. This presses upon the middle uterine artery and decreases the O<sub>2</sub> going to the fetus. If the case is neglected, the fetus dies and may undergo maceration or mummification.

UT can lead to occlusion of the blood circulation of the uterus and appendages, and placental ischemic injury can lead to decidual necrosis with vascular rupture and bleeding, followed by preterm labor and separation of the decidua and placenta [36]. Furthermore, severe acute UT can lead to placental abruption [37] and intrauterine fetal death [38].

The point of UT usually occurs at the level of the uterine isthmus [28], with three possible consequences (Fig. 11.2): (1) Rotation of the uterus may cause narrowing to complete obstruction of the birth canal. The fetus is unable to enter the cervix, stopping stage 2 of labor; (2) vascular compromise renders the uterine wall congested and fragile (Fig. 11.1); and (3) the diagnostic delay results in the delivery of a dead fetus since hypoxia can result from placental separation, due to venous congestion, even with intact membranes [39].

UT in the third trimester of pregnancy correlates with an abnormal fetal position, older





**Fig. 11.2** Posterior view of the uterus. (A) Fibroid situated upon the fundus of the uterus; (B) left broad ligament (wrapped around the body of the uterus); (C) right broad ligament; (D) rectum. (Reproduced with permission from [28])

maternal age, uterine ligament relaxation [40], or prepregnancy (partial) resection of broad ligaments due to endometriosis [41]. UT with a bicornuate uterus occurs between 21 and 33 weeks of gestation [38, 42–44]. This may be due to unilateral muscular attachments providing decreased stability and increased mobility, which puts the uterus at increased risk of UT [42]. Decreased uterine rotational stability can result in UT in subsequent pregnancies [41].

The causative factors in pregnancy are listed in Table 11.1.

11.3.3 Puerperium

The risk factors for UT during the puerperium include fixation of the uterus by adhesions, ovarian tumor, uterine myomas, large neoplasms, and uterine Müllerian anomalies. MRI evaluation following low transverse CS suggested that, occasionally, poor healing of the hysterotomy scar may result in suboptimal restoration of normal cervical length and strength, predisposing to UT [30]. Sometimes, the association of two or more factors determines UT—for example, uterus didelphys and iatrogenic adhesion between one of the uteri and the pelvic wall [14].

**Table 11.1** Causes of gravid uterus torsion [27, 28, 35, 38, 41, 45]

|                                                              |
|--------------------------------------------------------------|
| Uterine myomas                                               |
| Uterine anomalies, especially the bicornuate uterus          |
| Congenital weakness at the junction of the cervix and uterus |
| Previous cesarean section(s)                                 |
| Pelvic adhesions                                             |
| Abnormal pelvic architecture                                 |
| Ovarian neoplasms                                            |
| Abnormal fetal presentation or anomalies                     |
| Abnormalities of the spine or pelvis                         |
| Abdominal trauma                                             |
| Sudden maternal movements                                    |
| Peristaltic movements of the sigmoid colon                   |
| Bowel distension                                             |
| Excessive abdominal wall muscle contraction                  |
| External cephalic version                                    |
| Hydramnios                                                   |
| Multiple gestations                                          |
| Hyperactive fetus                                            |
| Interstitial pregnancy                                       |
| Resection of ligaments stabilizing uterus                    |
| No discoverable cause                                        |

11.4 Clinical Presentation

11.4.1 Pregnancy

11.4.1.1 Medical History

The clinical presentation of UT is variable and nonspecific. Symptoms depend on the [18] following:

- Degree of torsion,
- Speed at which the torsion develops,
- Duration of torsion,
- Stage of pregnancy, labor, or puerperium.

Therefore, the disease may be asymptomatic, acute, subacute, chronic, or intermittent. The severity of the disease ranges from asymptomatic to mild abdominal pain and cramping to shock and maternal death.

Asymptomatic cases (11%) [45] are mostly found during elective CS for other maternal [39] or fetal indications [46, 47], commonly fetal distress [19, 48, 49].

Asymptomatic UT is  $\leq 180^\circ$  [9, 46, 47].

The gradual type is usually  $90\text{--}200^\circ$  and often presents as obstructed labor [11]. The acute or fulminating type is usually  $\geq 180^\circ$ . The main clinical features are pain in the lower abdomen, shock (maternal pallor, tachycardia [11], breathlessness, and sweating [50]), intestinal and urinary symptoms, obstructed labor, and secondary vaginal bleeding due to placental abruption. In cases when clinical features exacerbate progressively, patients present with an acute abdomen. When gravid UT arrests the uterine circulation, it leads to acute maternal symptoms and threatens fetal survival. Thus, it is usually associated with placental abruption [51]. Other obstetric diagnoses can confound the examination, such as abnormal fetal heart rate [27, 49, 51–55] and failure to

progress in labor [53, 54, 56, 57]. Urinary symptoms include urgency, frequency, nocturia, oliguria, and hematuria. Pyrexia can result from red fibroid degeneration as a leading point of UT [12, 13]. UT presenting in labor [17] may manifest by the failure of cervical dilation despite strong uterine contractions or fetal distress due to a reduction in uterine blood flow. The symptoms are listed in Table 11.2, while symptoms related to the degree of UT are listed in Table 11.3.

11.4.1.2 Physical Examination

Examination reveals an abnormal pendulous shape of the abdomen [35]. The round ligament is palpably stretched across the maternal abdomen. Uterine hypertonia can be present with uterine tenderness on palpation. On pelvic examination, the uterine artery is perceived as pulsating anteriorly. A vaginal examination may reveal vaginal bleeding, uterine tenderness, spiral twisting of the vaginal or cervical canal with a high cervical position, stenosis of the vagina, uterine artery pulsating anteriorly, and urethral displacement [15, 58, 59]. The dorsal commissure of the vulva may be pulled forward and to the left or right (twisting of the vulva).

The transverse fetal lie is common with UT [35, 49, 60, 61].

Rectal examination reveals that the broad ligament on one side is pulled strongly downward and under the twisted uterine body and cervix. The opposite broad ligament is pulled tightly

**Table 11.2** Most common symptoms of gravid uterine torsion

| Symptoms at presentation                                    | n = 28 | % of symptomatic cases | % of total cases |
|-------------------------------------------------------------|--------|------------------------|------------------|
| Abdominal pain                                              | 23     | 82.1                   | 56.1             |
| Vaginal bleeding                                            | 3      | 10.7                   | 7.3              |
| Nausea/vomiting                                             | 4      | 14.3                   | 9.8              |
| Decreased fetal movement                                    | 4      | 14.3                   | 9.8              |
| Fetal distress                                              | 11     | 39.3                   | 26.8             |
| Hemodynamic instability/syncope                             | 12     | 42.9                   | 29.3             |
| Uterine size greater than dates or rapidly enlarging uterus | 3      | 10.7                   | 7.3              |
| Labor obstruction <sup>a</sup>                              | 2      | n/a                    | 4.9              |

Reproduced with permission from [11]  
<sup>a</sup> Both cases with labor obstruction had no other symptoms upon presentation

**Table 11.3** Symptoms (%) related to the degree of gravid uterine torsion

| Degree of torsion | Pain | Shock | Intestinal | Urinary | Bleeding | Obstructed labor <sup>a</sup> | Other symptoms | No symptoms |
|-------------------|------|-------|------------|---------|----------|-------------------------------|----------------|-------------|
| <90°              | 65   | 6     | 15         | 8       | 9        | 11                            | 20             | 14          |
| 90°–180°          | 75   | 18    | 14         | 8       | 11       | 16                            | 29             | 11          |
| >180°–360°        | 100  | 43    | 50         | 0       | 7        | 21                            | 21             | 0           |
| >360°             | 100  | 100   | 0          | 33      | 17       | 100                           | 0              | 0           |
| Unknown           | 100  | 50    | 0          | 0       | 0        | 0                             | 0              | 0           |

Reproduced with permission from [9]  
<sup>a</sup> Although obstructed labor was not mentioned in any of the cases with torsion of  $>180^\circ$ , it could nevertheless be a factor in all such cases

across the uterine body and cervix. John Grønkjær Jensen described four pathognomonic clinical findings of UT [9]:

- Round ligament palpably stretching across the abdomen,
- Uterine artery pulsating anteriorly on vaginal examination,
- Twisting of the vagina or the cervical canal with the urethra displaced laterally,
- Twisting of the rectum.

In addition to the clinical presentation, unsuccessful labor induction should raise the suspicion of UT. The failure of the uterus to respond to oxytocics is due to ischemia of the myometrium [42].

11.4.2 Puerperium

The clinical presentation of puerperal UT is non-specific and may differ from UT during pregnancy. The most common symptom is abdominal pain varying from mild abdominal tenderness to symptoms of an acute abdomen, making diagnosis difficult. In the puerperium, a significant decrease in postpartum discharge (*lochia*) and a sudden complete stop of vaginal bleeding and discharge several days after delivery are highly suggestive of puerperal UT [14].

11.5 Differential Diagnosis

Due to the rarity, the nonspecific clinical presentation with variable severity makes correct preoperative diagnosis challenging. The differential diagnoses are presented in Table 11.4.

**Table 11.4** Differential diagnosis of gravid uterine torsion [6, 16, 62]

|                                       |
|---------------------------------------|
| Ectopic pregnancy                     |
| Acute hydramnios                      |
| Obstructed labor                      |
| Placental abruption                   |
| Abdominal hemorrhage                  |
| Torsion of a pelvic tumor             |
| Peritonitis                           |
| Concealed accidental hemorrhage       |
| Tonic uterine contraction             |
| Degenerating fibromyomata             |
| Uterine retroversion or incarceration |
| Uterine inversion                     |

11.6 Diagnosis

The preoperative diagnosis of UT is challenging, and the diagnosis is primarily intraoperative. Up to 1948, there was no instance of this condition being diagnosed preoperatively [63]. A severe UT can cause irreversible ischemic injury, thrombotic accidents, and fetal wastage. Hence, it is crucial to diagnose this condition quickly. In women who are known to have uterine anomalies that have acute severe abdominal pain in pregnancy, the possibility of UT should be considered. When fetal distress without a known cause is present, asymptomatic UT should be excluded [19, 48].

11.6.1 Laboratory Findings

There is no specific laboratory test for UT. Leukocytosis is present, especially if UT is complicated, such as uterine rupture [38]. Low hemoglobin levels are present with associated bleeding, as with placental abruption or uterine rupture. The severity of maternal shock is mostly greater than expected for the initial hemoglobin level [64]. Maternal serum alpha-fetoprotein (MSAFP) screening was originally used to detect

aneuploidy and fetal malformations such as neural tube and abdominal wall defects. Also, MSAFP elevation in the second trimester is associated with an increased risk of pregnancy complications and adverse obstetrical outcomes, including pre-eclampsia, preterm labor, intrauterine growth restriction, intrauterine fetal demise [65], and even UT [38]. A proposed explanation for this finding in the context of a structurally normal fetus includes fetal-placental insufficiency [66].

### 11.6.2 Plain Abdominal X-Ray

On plain abdominal radiographs, gas in the uterine cavity has been described as a feature of UT in a nongravid patient [67]. Possibly, it can be applied to the gravid uterus, but no images exist in the literature.

### 11.6.3 Abdominal Ultrasound

Ultrasound (US) is not specific for UT in pregnancy. Comparison with previous US scans can reveal fibroids that have changed position, implying a torsion of a myomatous uterus [67]. Also, a change in placental position [31, 61, 68] or abnormal position of ovarian or uterine vessels

across the uterus on the Doppler examination [68] may be signs of UT. The hyperechoic area behind the placenta suggests placental abruption, and UT was never a working diagnosis [37, 38, 56, 69]. No US images of gravid UT exist in the literature.

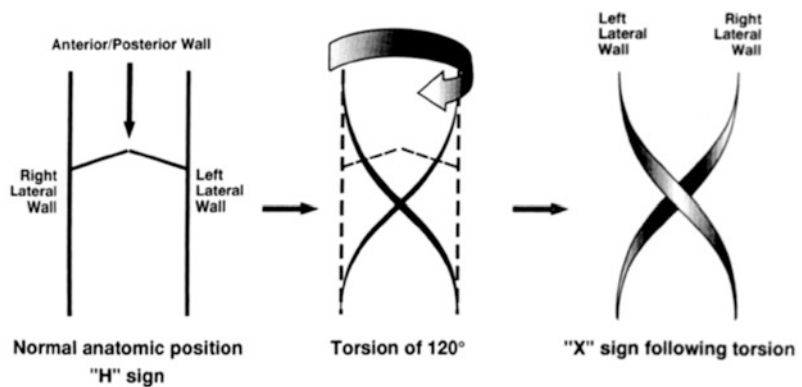
### 11.6.4 Abdominal CT

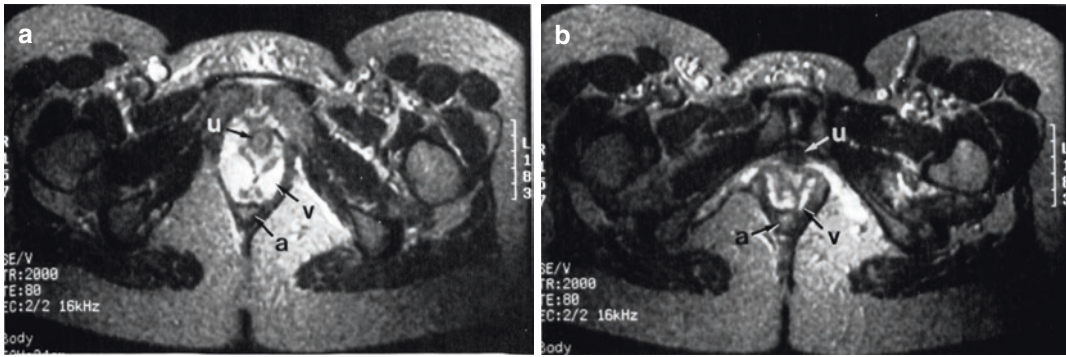
On an abdominal CT, gas in the uterine cavity is a feature of UT in a nongravid patient [67]. It can be applied to the gravid uterus, but no images exist. This diagnostic imaging is rarely performed because the indication for exploration or CS is based on the emergent clinical findings of maternal acute abdomen, shock, or fetal distress.

### 11.6.5 Abdominal MRI

Emergent MRI provides an accurate evaluation when the equipment and personnel are available. Nicholson et al., in 1995, detected the first case of UT in pregnancy by MRI [70]. The wall of the upper vagina changes from a normal H configuration to an X-shaped configuration in UT (Figs. 11.3 and 11.4), but the plane should be at the level of the vagina on abdominal MRI [71].

**Fig. 11.3** Schematic representation of uterine torsion at the level of the upper vagina. (Reproduced with permission from [70])





**Fig. 11.4** Transverse section MRI of the vagina (v), urethra (u), and anal canal (a). (a) Distorted anatomy in uterine torsion (X-shaped configuration). (b) Normal anatomic position at the level of the inferior vagina

(H-shaped configuration). The lower vagina is fixed at the introitus, so the normal H-shaped configuration is maintained. (Reproduced with permission from [70])

## 11.7 Treatment

UT in pregnancy is an absolute indication of emergent operation due to several goals:

- Prevent or stop uterine ischemia,
- Prevent or stop the adnexal ischemia,
- Prevent placental abruption due to venous stasis and ischemia,
- Prevent or stop fetal hypoxia/anoxia.

In animals, non-surgical methods are (1) rotation of fetus and uterus when hands may pass through the twisted portion (for lesser degree torsion), (2) very fast rolling, and (3) rolling using plank (*Schaffer's method*).

If the diagnosis is known or suspected preoperatively, the patient could be offered simultaneous tubal ligation [34]. These situations include when no further pregnancies are planned or to eliminate the risk of similar complications in subsequent pregnancies.

### 11.7.1 Operative Treatment

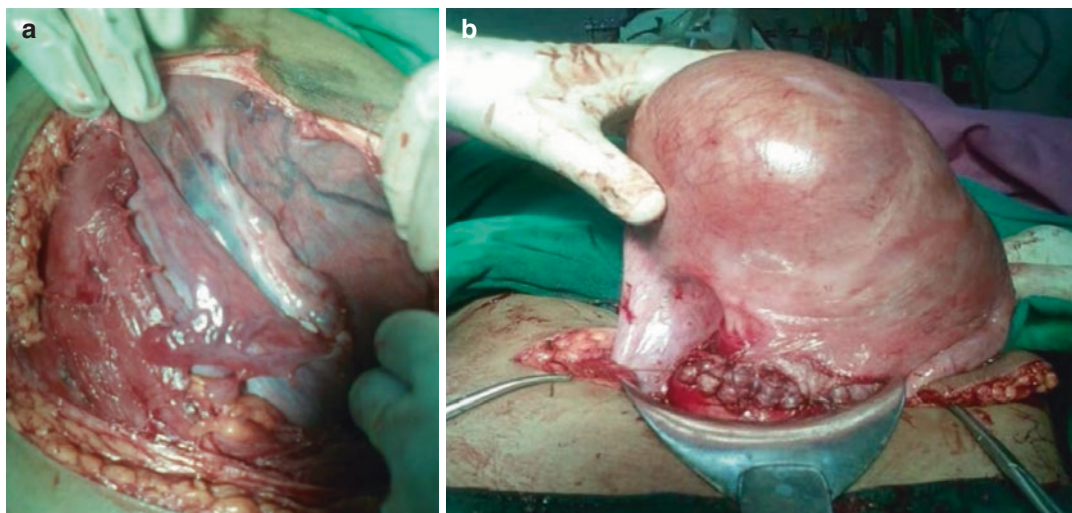
#### 11.7.1.1 Uterine Detorsion

The only therapy for a successful maternal and fetal outcome is laparotomy, CS, and UT correction (Figs. 11.5, 11.6, 11.7, and 11.8). During exploration, the anterior aspect of the uterus has

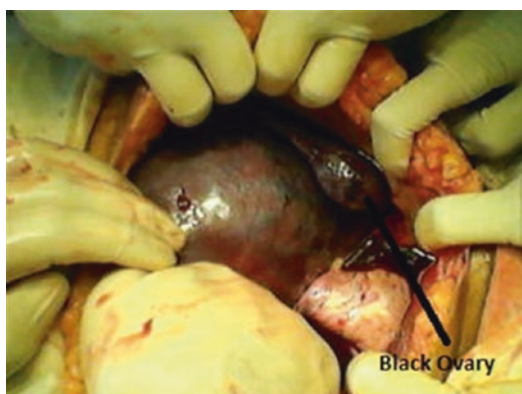
abnormal implantation of the uterine adnexa, which is morphologically identical to the normal posterior aspect of the uterus implicating UT [74]. Adnexa is commonly congested [75] or could even be ischemic/necrotic [75, 76]. With UT, the uterovesical fold cannot be identified [59, 77], dilated veins on the lower uterine segment (Fig. 11.1), and excessively stretched round ligament that crosses the midline are present. The routine practice of palpating the round ligament at the time of CS would most likely prevent inadvertent hysterotomy at sites other than the anterior lower segment [43]. With previous delivery by CS, bladder adherence to the lower aspect of the posterior surface of the uterus (torsion of 180°) would suggest that the UT could have taken place in the previous pregnancy just after CS [39]. With uterus didelphys, the torsion of one horn is easier to detect (Fig. 11.7). The vitality of the uterus is checked after detorsion. Detorsed parts (horn, one side of uterus didelphys) atonic after intraoperative uterotonics should be resected [43].

After detorsion, or even prophylactically after CS in patients with risk factors for UT, the uterus fixation in the usual anatomic position is questionable. Bilateral plication of the uterosacral ligaments prevents immediate postpartum recurrence of UT [69, 71]. This may help keep the uterus in its natural position and reduce the effect of iatrogenic uterine adhesion. It may provide





**Fig. 11.5** (a) posterior wall uterus with vital left adnexa turned to right; (b) detorsed uterus with myoma after suturing. (Reproduced with permission from [72] under the CC Attribution License)



**Fig. 11.6** Gangrenous ovaries due to venous stasis caused by 360° torsion of a 17-week pregnant uterus with myoma. After detorsion, ovaries became vital. (Reproduced with permission from [73])

resistance to UT and prevent long-term recurrence [78]. The third option is the bilateral plication of the uterosacral and round ligaments [9]. With UT recognized at term and successful manual detorsion, CS with standard *anterior Cesarean hysterotomy* is recommended.

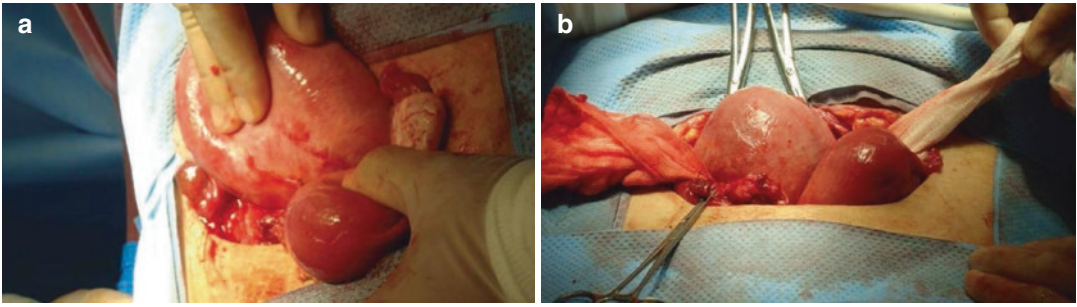
### 11.7.1.2 Hysterotomy

Sometimes the detorsion is initially impossible, especially near the term. Then, the hysterotomy in the form of CS allows detorsion after delivery of the viable or nonviable fetus [35, 43]. It is

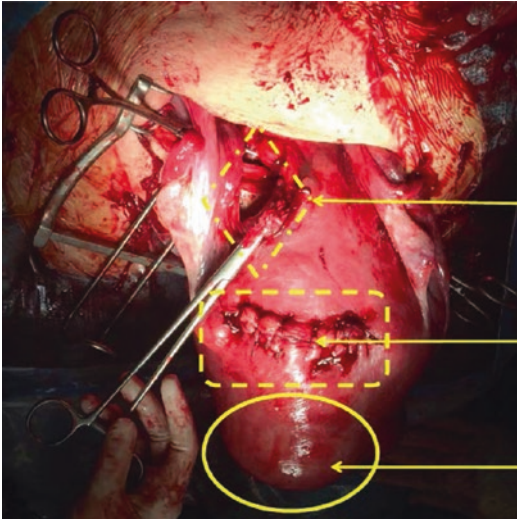
important to note the position of round ligaments anteriorly before hysterotomy. If UT is not identified, the incision would be given inadvertently in the lateral wall of the uterus, leading to hematoma formation. Both vertical and transverse posterior uterine incisions are indicated depending on the circumstances.

The *posterior vertical Cesarean hysterotomy* is recommended when the lower segment of a twisted uterus is inaccessible due to dense adhesions or covered with engorged venous vessels [9]. Sometimes, the low transverse incision cannot be made due to a narrow and twisted lower uterine segment, and a vertical incision is the only option [34, 64]. It also minimized the risk of ureteral injury. In these cases, a classical posterior hysterotomy should carry the least risk of injury to vascular structures of the broad ligament.

On the other hand, the risk of rupture, blood loss, and operating time of a *posterior transverse cesarean hysterotomy* are theoretically less than a posterior vertical incision [35]. The data on the long-term consequences of posterior uterine incisions, particularly on the outcome of subsequent pregnancies, do not exist [35, 79, 80]. The anatomical landmarks should be defined before the uterine incision to prevent accidental injury to blood vessels or other



**Fig. 11.7** Vital post-Cesarean section uterus didelphys: (a) before detorsion, and (b) after detorsion. (Reproduced with permission from [14] under the CC Attribution License)



**Fig. 11.8** Exteriorized uterus after untwisting, posterior side. Opening of the right broad ligament and section of the branches of the right uterine artery (*rhombus*). Posterior transversal hysterorrhaphy (*rectangle*). Myoma below hysterorrhaphy (*ellipse*). (Reproduced with permission from [47])

organs. After delivery, manual correction is easy. Any predisposing factors such as adhesions, fibroids, or ovarian cysts should be removed to prevent a postpartum recurrence. After deliberate posterior transverse cesarean hysterotomy, the round ligament plication may prevent recurrent UT in the immediate puerperium [71, 81]. Incorporating into routine practice the palpation of round ligaments at the time of CS would most likely prevent inadvertent hysterotomy at sites other than the anterior lower segment [10]. The uterine incision is closed in a standard fashion (Fig. 11.8) with a

double layer of delayed-absorbable suture (polyglycolic acid suture 2-0).

Uterotonics are given to estimate the vitality of the uterus [82]. A hysterectomy is recommended if the uterus is atonic and nonviable, with the potential of necrosis or subsequent bleeding [64, 82].

Some administer uterotonics for intrauterine fetal death before hysterotomy to minimize bleeding [82], while others give uterotonics after hysterotomy and the extraction of the dead fetus [64].

### 11.7.1.3 Hysterectomy

Hysterectomy is indicated if [83, 84]:

- The uterus is not viable,
- Women past the reproductive age,
- Women do not desire more pregnancies,
- Unsuccessful uterotonics during the third stage of labor.

It is, however, challenging to determine whether the ischemic injury affecting the uterus is reversible, especially because puerperal UT is rare [14]. When low hemoglobin is encountered, and the fetus is dead, bilateral uterine artery ligation before proceeding with conventional CS after untwisting the uterus reduces intraoperative

blood loss [85]. The ischemic single-sided uterus of twisted uterus didelphys bicollis mandates one-side subtotal hysterectomy (commonly with ipsilateral adnexectomy due to gangrenous changes) to preserve fertility [58, 77].

### 11.7.2 Obstetric Management

Obstetric decisions depend on gestational age. Beyond 34 weeks, CS is the procedure of choice. At an earlier stage (before 23–24 weeks), the causative factor should be corrected if possible, and the pregnancy is allowed to continue to term. In the interval between the limit of fetal viability at 23–24 weeks' gestation and the 34th week or the rare instance when imaging accurately establishes the preoperative diagnosis and signs and symptoms are not compelling, the best management is unclear. After successful uterine derotation into the anatomic position, the gynecologist must balance the unknown risk of maternal or fetal complications if the delivery is not accomplished against the immediate risk of substantial prematurity.

## 11.8 Prognosis

### 11.8.1 Maternal Outcome

#### 11.8.1.1 Morbidity and Mortality

During the 1970s, the maternal mortality rate associated with gravid UT was 13%, and when UT was accompanied by malpresentation, the mortality rose to 20%. Mortality is directly related to the duration of gestation and the degree of UT. Under 5 months, it was 0%, whereas at term, it reached 18.5% [9, 32, 52]. In 1951, it was 7.4% in UT of 90–180° and increased to 50% when it was 180–360° [9, 76]. Until 1960, for UT >180, maternal mortality was 44% [9]. Between 1960 and 1976, only one mother died [9]. The two last cases of maternal mortality were in 2005 (the delay in UT treatment) [68] and 2020 (prolonged hemorrhagic shock) [86]. Since 2006, the maternal outcome in twin pregnancies is not increased [33]. Table 11.5 shows maternal mortality from 1876 to 2020.

**Table 11.5** Maternal mortality with gravid uterine torsion (1876–2020) [9–11, 33]

| Year      | Recovery (%) | Fatal (%) | Unknown (%) | Torsion >180° (%) |
|-----------|--------------|-----------|-------------|-------------------|
| 1876–1899 | 57           | 29        | 14          | 0                 |
| 1900–1929 | 83           | 17        | 0           | 13                |
| 1930–1959 | 89           | 11        | 0           | 16                |
| 1960–1990 | 98           | 1         | 1           | 1                 |
| 1966–2006 | 97.4         | 2.6       | 0           | No data           |
| 2006–2020 | 97.5         | 2.5       | 0           | 7.3               |

Pulmonary embolism has been described after uterine detorsion [51, 56].

#### 11.8.1.2 Future Pregnancy

The women with UT treated without hysterectomy have normal fertility and can have normal future pregnancies. There are no evidence-based recommendations for women who have had a UT and wish for future pregnancies. The risk of uterine rupture with a prior posterior lower segment incision versus the risk following an anterior lower segment incision remains unknown. Recommendations following vertical posterior hysterotomy for future pregnancies are similar to anterior classic CS [47, 48]. Theoretically, a repeated CS is safer because it avoids the possibility of a labor-associated uterine rupture [10] or repeated UTs. Between 1966 and 2006, 2/36 cases had described subsequent pregnancies. Both had successful CS [10].

### 11.8.2 Fetal Outcome

Perinatal mortality increases with the following:

- Higher UT degree,
- Longer UT duration,
- Uterine malformations,
- Increasing gestational age until midgestation,
- Earlier decades during the twentieth century.

Until 1956, it was 24% when the uterus was rotated 90–180° and reached 75% with torsion

of  $>180^\circ$  [45]. Then, until 1992 it was 20% for  $UT \leq 90^\circ$ , 71% for  $90-180^\circ$ , 71% for  $180-360^\circ$ , and 83% for  $>360^\circ$  [9]. It declined from 37.5% from 1876 to 1911 to 24.1% from 1941 to 1956 [45]. The fetal mortality rate of 18% in (English language reports) cases from 1966 to 2006 [10] was higher than 12% reported (in a variety of countries) from 1876 to 1992 [9]. Since 2006, perinatal mortality has been 22% [11]. Gestational age has also been found to impact perinatal outcomes. Perinatal mortality was 19% before the fifth month, 50% in the fifth to sixth, 35% in the seventh to eighth, and 19% at term [9, 45]. UT associated with uterine malformations (bicornuate uterus, uterus didelphys, etc.) is also associated with other adverse pregnancy outcomes like preterm labor, IUGR, a spontaneous uterine rupture, and obstructed labor due to the rudimentary horn [43, 64]. Since 2006, only two cases have been reported on IUGR [33]. It can be underreported, or the incidence is low due to the acuity of the condition without enough time for IUGR to develop. Since 2006, twin pregnancies have not increased fetal mortality [33].

There are no data about fetal morbidity. During UT, blood supply is decreased to the uterus. Initially, obstruction of venous blood flow raises the pressure in the placental cotyledons, leading to fetal distress and abruption. If arterial blood flow is compromised, fetal demise may ensue [72]. Therefore, increased fetal morbidity is expected. There are cases of clubfeet deformity [80].

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# Symptomatic Uterine Myoma

# 12

## Abstract

Uterine fibroids (leiomyomas or myomas) are the most common benign uterine neoplasms, especially over the age of 30. Myomas are increasingly found in pregnancy because many women delay childbearing. Uterine myoma can be asymptomatic or symptomatic. Presentations include red degeneration, spontaneous bleeding, obstructed labor, fibroid torsion, and gravid uterine torsion. It is essential to define the type of uterine myoma presentation. All presentations can be defined by transabdominal or transvaginal sonography. Abdominal MRI is used in unequivocal cases. Bleeding myomas are treated with radiologic or surgical interventions. Red degeneration is treated conservatively based on analgesia. Torsion of the gravid uterus should be detorsed immediately to minimize fetal hypoxia and death. The potential of obstructed labor is a complex issue that should be diagnosed before the labor starts to prevent emergency obstetric interventions.

## 12.1 Definition and Classification

Uterine fibroids (UF), also known as leiomyoma or myoma, is the most common uterine neoplasm, especially over the age of 30. These benign monoclonal tumors of smooth muscle

origin have varying amounts of fibrous connective tissue [1]. UF usually arise in the myometrium and occasionally in the cervix, broad ligament, or ovaries [1, 2]. UF are multiple in up to 84% [3], with prevalence increasing with age, from 40–60% at 35 years to 70–80% at 50 years old. The highest prevalence is in black women, who also often have the more severe disease [4, 5]. UF usually decrease in size after menopause. Early age at menarche and obesity are risk factors for developing UF, likely due to increased exposure to estrogen [6].

UF are classified according to their location as submucosal, intramural, or subserosal [1]. *Submucosal fibroids* are the least common, accounting for 5% of UF [7], but are most likely symptomatic since they project into the endometrial cavity. Submucosal fibroids can become pedunculated and prolapse into the cervical canal or vagina [8]. *Intramural fibroids* are the most common but usually asymptomatic; however, they may cause infertility due to compression of the fallopian tubes. *Subserosal fibroids* project exophytically into the abdomen or pelvis and can become pedunculated and confused with ovarian tumors.

Large UF often degenerate as they outgrow their blood supply. Dead UF cells are often replaced by collagen. This type of degeneration is called *hyaline degeneration*. Degeneration in UF may be hyaline (the most common), myxomatous, cystic, fatty, hemorrhagic, or malignant

[7, 9, 10]. The type of degenerative change depends on the degree and rapidity of the onset of vascular insufficiency. Calcification tends to occur following necrosis [10].

Although most UF are benign, some uterine leiomyosarcomas arise in a subset of UF [11]. Only 0.23–0.7% of benign UF turn out to be leiomyosarcomas on pathologic examination [12, 13]. Most leiomyosarcomas arise de novo. A leiomyosarcoma can be difficult to distinguish from a benign UF, particularly during rapid UF growth.

larger sizes, because of their removal before pregnancy [14]. UF affect 0.1–12.3% of pregnant women [14, 17–20]. The prevalence differs with ethnicity (Fig. 12.1) (18% in African–American women, 8% in white women, and 10% in Hispanic women) [21]. In older women undergoing ovum donor-recipient in vitro fertilization (IVF), the incidence rises to 25% [22, 23].

The inaccuracy of different UF types or locations during pregnancy is due to the lack of data. The pedunculated UF were reported in 11%, subserosal or intramural UF in 7.6%, and in the remaining cases, the UF type was not reported [24].

## 12.2 Incidence

*Edema and softening may result from changes during pregnancy.*

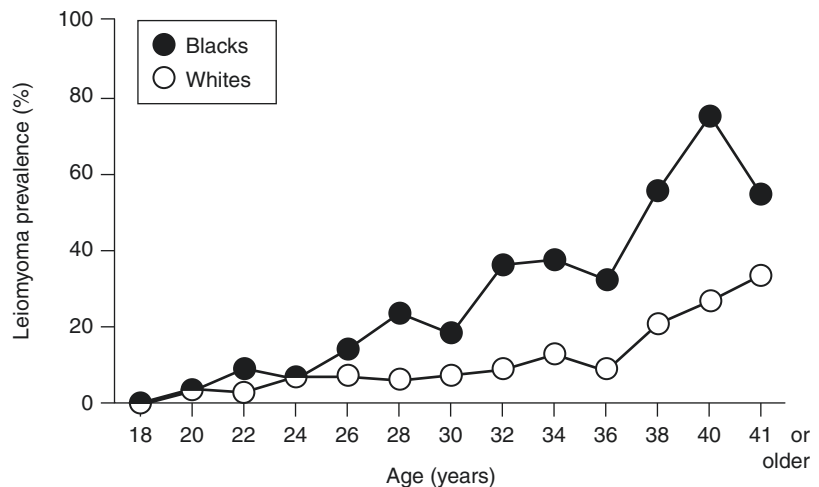
(Adolf Ludwig Sigismund Gusselow, 1885)

The mean maternal age is higher among women with UF than in the general obstetric population [14]. In Canada, for all births, the average age of mothers at childbirth has been over 30 since 2010 (30.8 years in 2016). The average age of mothers at first birth was 28.7 years in 2012 and 29.2 years in 2016. It has been rising steadily since the mid-1960s [15]. This resulted in an increased UF occurrence in pregnancy [3, 16]. In contrast, others claim the decreasing incidence of submucosal UF during pregnancy, especially in

### 12.2.1 Red Degeneration

Enlarging UF can outgrow its blood supply and undergo degeneration (muscular infarction). Red degeneration (aseptic necrobiosis, carneous degeneration, and hemorrhagic infarction) is common during pregnancy. Even before 1913, a relationship between red degeneration of UF and pregnancy was evident [25]. In the 1920s, the estimated occurrence was 0.7% [26]. Monro Kerr and Chassar Moir found an incidence of 0.8%. Between 1930 and 1954, the incidence was approximately 0.35% [27]. The incidence of UF during pregnancy varies greatly from 0.01%

**Fig. 12.1** Prevalence of uterine myomas during the first trimester among Black and White Women. Prevalence is for 2-year intervals (18 = 17 and 18-year-olds; 20 = 19 and 20-year-olds, etc.). Patients with assisted reproduction techniques are excluded. (Reproduced with permission from [21])



[19] to 1.6–2% [28]. A significant number of patients gave a history of infertility (43%) and spontaneous abortions (25%) [19]. Having an accurate number of red degeneration cases is complex [29].

### 12.2.2 Spontaneous Bleeding

Spontaneous hemoperitoneum is extremely rare despite increased vascularization of the uterus during pregnancy and up to 12.3% of the pregnant woman with UF [14, 17–20]. Carl von Rokitansky reported the first case discovered at the autopsy of a girl who had died from internal abdominal bleeding. It is rare even in the general female population, with 125 cases published from 1902 to 2020 [30]. The numbers could be higher because Hasskarl, in 1949, collected 60 cases [31].

Ernest Lambert published the first cases of pregnancy in 1870 and Gaillard Thomas in 1875. Adolf Ludwig Sigismund Gusselov, an editor of the journal *Archives of Gynecology*, in 1878, described a 27-year-old pregnant woman in a profound shock that resulted in death from bleeding UF. Spontaneous abortion of a 4-month dead fetus took place 40 h before symptoms [32]. Until 2020, 115 cases of spontaneous bleeding from UF in the general population have been collected [30], while over 20 were during pregnancy [32–47].

### 12.2.3 Uterine Fibroid Torsion

The first descriptions were by Carl von Rokitansky, Turner, and then James Cappie, who presented the fatal case at the Obstetrical Society of Edinburgh in 1874 and published it in 1875 [48]. UF torsion during pregnancy is exceptionally rare [48–53].

### 12.2.4 Gravid Uterus Torsion

See Chap. 11.

## 12.3 Natural History

*Large or multiple fibroids exert pressure on ... the uterus itself... and hence an enlargement of the blood vessel which may be further stretched and occasionally be torn. In this manner, it has been noted that a tear of a subserosal vein in a fibroid led to hemorrhage into the peritoneal cavity.*

(Karl von Rokitansky, 1861 [54])

### 12.3.1 Uterine Fibroid Growth

Most ultrasound (US) studies have shown that most of the UF during pregnancy (60–78%) do not show significant changes in their volume. UF that did increase their volume (22–32%), the growth was limited to the first trimester [55]. UF increases  $12 \pm 6\%$  of the initial size, up to 25%. At 4 weeks postpartum, the size of the UF did not differ significantly from the size during pregnancy [55]. However, the magnitude of UF enlargement differs across studies [56, 57]. In one study, the volume of the UF more than doubled within 6–7 weeks' gestation [58]. One case showed normal pregnancy without any signs of UF during five gestational weeks. At the seventh week of pregnancy, a 3.5-cm subserosal UF was found. At the 12th week of pregnancy, the US showed a subserous pedunculated UF  $15 \times 10.9$  cm on the left edge of the uterine fundus [59].

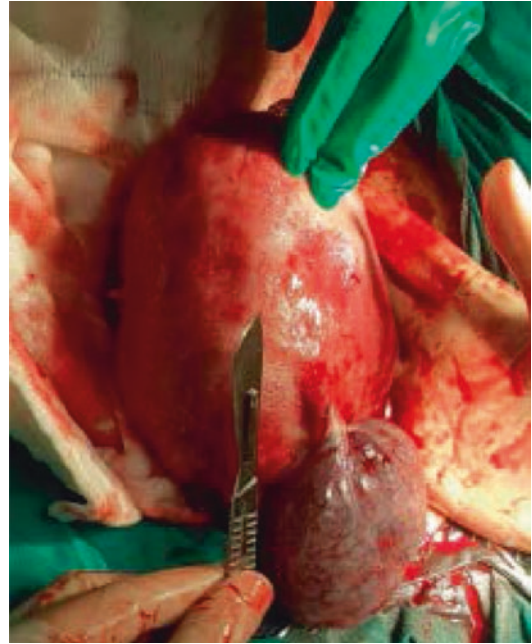
Differently, there are contradictory data about the modifications of UF during the second trimester of pregnancy. The most likely is a nonlinear trend of growth of UF. UF may undergo a progressive slowdown during the second trimester, up to stabilization and subsequent regression. Some UF may start to reduce in size earlier (at the beginning of the second trimester) and others significantly later (during the second half of gestation), probably concerning their initial size (with larger lesions starting to reduce in size earlier in comparison to smaller lesions) [56].

Similarly, discrepancies exist for UF growth during the third trimester. Some claim that UF increase in size, while others claim to decrease.

The third option is that small UF (<4 cm) enlarge or do not change, while UF >4 cm decrease in size [56].

Infarction of UF secondary to uterine involution in the postpartum period facilitates this complete regression of small UF in puerperium [60]. This is supported by epidemiologic data that parity is protective against the incidence and further development of UF [4].

The remarkable growth of UF during the initial pregnancy could be related to other pregnancy-related hormones rather than sex steroids because serum concentrations of estrogen and progesterone are higher in the second half of pregnancy [58, 61]. One hypothesis is that the “LH-hCG myomal receptors hyperstimulation” due to serum embryonic-hCG increases in early gestation [61]. Nevertheless, given the possible histological heterogeneity of UF in terms of the percentage of smooth muscle cells and collagenous matrix, the expression of LH receptors may differ, leading to a wide range of sensitivity to hCG stimulation [58]. However, many other hormones, enzymes, and growth factors secreted by the maternal and fetoplacental compartments markedly increase during early pregnancy, with potential effects. Similarly, factors such as UF–placental site relationship and UF location (submucosal, intramural, or subserosal) may influence their growth trend [56].



**Fig. 12.2** Twisted subserosal pedunculated uterine fibroid in the 35th week of pregnancy. Excision with Cesarean section was performed. (Reproduced with permission from [51] under the CC BY 4.0)

severe abdominal pain. Torsion is more likely in the first trimester [64] and after delivery [53] when a large space in the abdominal pelvic cavity permits UF twisting, although it can develop throughout pregnancy [51].

### 12.3.2 Acute Red Degeneration

Acute red degeneration of a UF occurs almost exclusively during pregnancy. It usually occurs between the tenth and 20th weeks, during the fastest uterine growth [19, 62]. The first trimester is a period of the most significant UF growth. Rapid UF growth can result in a relative decrease in perfusion, leading to ischemia and necrosis (red degeneration) and the release of prostaglandins, causing pain [63].

### 12.3.3 Uterine Fibroid Torsion

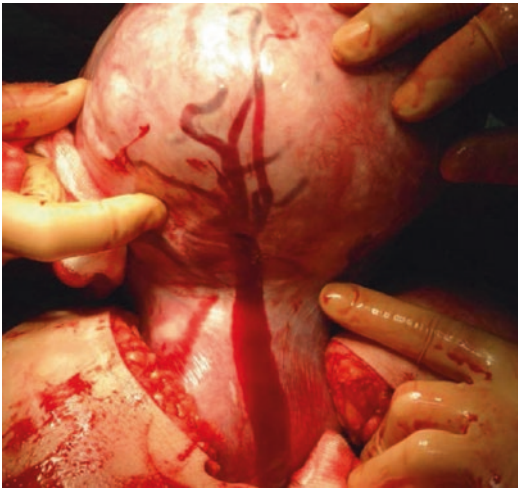
Pedunculated subserosal UF can undergo torsion and consequent infarction (Fig. 12.2), resulting in

### 12.3.4 Spontaneous Bleeding

Spontaneous bleeding UF during the first trimester [35, 37] or a term or the immediate postpartum period is most common [33, 34, 38, 41, 43, 44], although sporadic cases are present throughout pregnancy [36, 46, 47]. The hypothesis is that involution of the uterus after delivery promoted compression of venous drainage but not arterial flow [41, 44]. Spontaneous bleeding presents as (1) free subserosal UF bleeding into the abdominal cavity (Fig. 12.3) or (2) intrafibroid bleeding resulting in fast-growing, very large UF (Fig. 12.4) commonly with underlying red degeneration [41]. Bleeding can also result from UF rupture [65, 66].

Subserosal UF are prone to free intra-abdominal bleeding [37]. The risk factor for spon-





**Fig. 12.3** A 10-week gravid uterus with pedunculated myoma. Large ruptured vein causing massive intra-abdominal bleeding. (Reproduced with permission from [35] under the CC BY 2.0)



**Fig. 12.4** Rapidly growing uterine fibroma extirpated during puerperium. The cut surface shows a dark red area of bleeding. (Reproduced with permission from [44])

taneous intrafibroid bleeding is red degeneration [44]. This could lead to blood sequestration from maternal circulation into large UF, resulting in hypovolemia without hemoperitoneum [30]. The venous drainage of large UF courses over their surface and enters the supporting myometrium at the periphery of the UF. In most cases, the bleeding occurs from torn, enlarged veins coursing over the surface of subserosal UF [37, 67]. A sudden increase in venous pressure is a risk factor for venous bleeding: Uterine manipulation [33], straining at stool, lifting heavy weights, and violent coitus can provoke bleeding. In pregnancy,

posterior wall UF are at higher risk, as trauma or delivery from direct contact with the sacral promontory can result in rupture and hemoperitoneum [33]. The dual effect of increased vascularity and venous congestion with mechanical extrusion of the UF can aggravate the condition and the force of tension created on the surface of the UF. This can lead to a tear of the superficial veins [67].

### 12.3.5 Uterine Incarceration

See Sect. 28.1.

## 12.4 Clinical Presentation

### 12.4.1 Medical History

Most UF are small and remain asymptomatic. However, 10–40% will have symptomatic UF-related complications in pregnancy [68], with at least some discomfort. Very large UF can change the shape of the abdomen or present with lumps (Fig. 12.5). More than 50% present with abdominal pain without bleeding [68]. Approximately 5–21% require hospitalization during pregnancy for pain control [69], and >25% with UF >5 cm experience pelvic pain of significant intensity to require narcotic analgesics [20].

The pain of UF acute red degeneration is often sudden, severe, and localized to the site of the UF, usually in the pelvic area. The severe pain often lasts for 2–4 weeks. Unlike torsion of an ovarian mass, there is no direct correlation between the size of the UF and the degree of pain, but most UF associated with abdominal pain have a volume >200 cm<sup>3</sup> [70]. Vomiting and dehydration are self-limiting. A similar presentation is found with UF torsion [49, 51, 64].

Bleeding presents as intra-abdominal bleeding, including intrafibroid bleeding or vaginal bleeding. Vaginal bleeding mainly correlates with UF position and size, especially if >5 cm [20]. Intra-abdominal bleeding is the rarest presentation. Depending on the bleeding severity, only falls in hematocrit and hemoglobin can be detected [35], or hypovolemic shock results from massive free intra-abdominal bleeding.



**Fig. 12.5** Umbilical lump (arrow) from the large uterine fibroid at 39 weeks of pregnancy. (Reproduced with permission from [72] under the CC Attribution License)

Intestinal obstruction from large UF presents with nausea, vomiting, the absence of stool and flatus, and abdominal distension [71].

Acute urinary retention results from (1) direct compression of the urinary bladder by UF or (2) UF causing uterine retroversion with resultant acute urinary retention (see Sect. 28.1). This is found in 5% of symptomatic UF [19].

12.4.2 Physical Examination

With acute UF red degeneration or UF torsion [64], an exquisitely tender abdomen with signs of localized peritoneal irritation is common. The tenderness is over the mass attached to the uterus. Fever can be present. The typical presentation of red degeneration is present in 50% of patients [19]. Large UF can compress the lower genital tract. In 1896, Richard Douglas wrote *I made a digital and specular examination, was unable to find the os uteri. The right vaginal vault and iliac region were filled with a hard tumor* [73].

With torsed subserosal pedunculated UF, obstetric (including non-stress test) and vaginal examinations are normal [51, 64].

12.5 Differential Diagnosis

Differential diagnoses depend on the presentation of the UF. Uterine incarceration is a differential diagnosis of painful or degenerating UF [74].

**Table 12.1** Common differential diagnosis of red degeneration in pregnancy

| Surgical            | Gynecologic           |
|---------------------|-----------------------|
| Acute appendicitis  | Hydatid mole          |
| Acute cholecystitis | Adnexal torsion       |
| Acute pancreatitis  | Torsion of the cyst   |
|                     | Uterine incarceration |
|                     | Placental abruption   |
|                     | Ovarian tumor         |

Incarceration is when the uterus is fixed in the hollow of the sacrum wedged between the sacral promontory and pubic rami, unable to leave the pelvis. This condition is rare and ranges from 1/3000 to 1/10,000 pregnancies [74], and unlike UF, it can lead to fetal growth restriction. The abdominal US or MRI can confirm the diagnosis (see Sect. 12.6). The most common differential diagnoses of red degeneration are in Table 12.1. Differential diagnoses of intestinal obstruction are in Chap. 18 and acute urinary retention in Sect. 28.1.

12.6 Diagnosis

UF is easy to detect with diagnostic imaging. Unfortunately, 96% of bleeding UF in the general population had a preoperative diagnosis of intra-abdominal bleeding of unknown origin. The intraoperative incidental finding was a UF [30]. The preoperative diagnosis of bleeding UF in pregnancy is exceptionally rare [36, 41]. Pregnant women with UF should undergo frequent US evaluations during pregnancy to monitor fetal growth and UF size [14].

12.6.1 Laboratory Findings

Laboratory findings depend on the cause of symptomatic UF. Leukocytosis and elevated CRP are common with UF torsion [51, 64, 75] and red degeneration. Fall in serum hemoglobin and hematocrit results from intra-abdominal or intrafibroid bleeding of large UF [35]. UF torsion rarely results in bleeding and a fall in serum hemoglobin and hematocrit.

12.6.2 Abdominal Ultrasound

The abdominal US is the first imaging modality in evaluating UF during pregnancy. It determines the number, localization, vascularization, shape, and relationship between UF and the uterine cavity. The US of a degenerating UF shows a well-circumscribed uterine mass composed of echodense and echolucent areas (Fig. 12.6). A sharp drop in residence index in Doppler means some degree of necrosis [76]. As pregnancy progresses, the UF may become

inaccessible as they become soft, flattened, and indistinct due to interstitial edema, often confused with fetal parts.

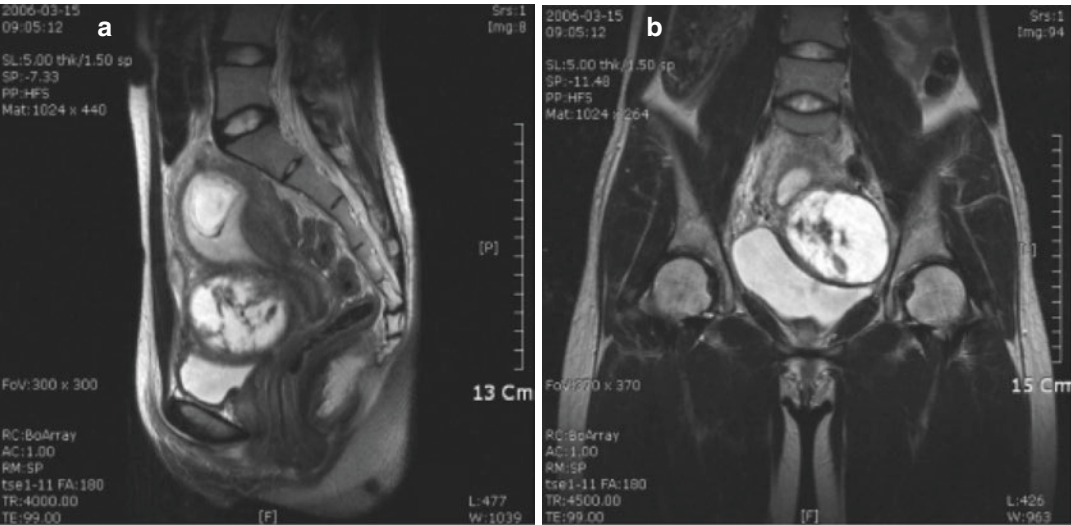
The US Doppler defines the indication for myomectomy during pregnancy [76].



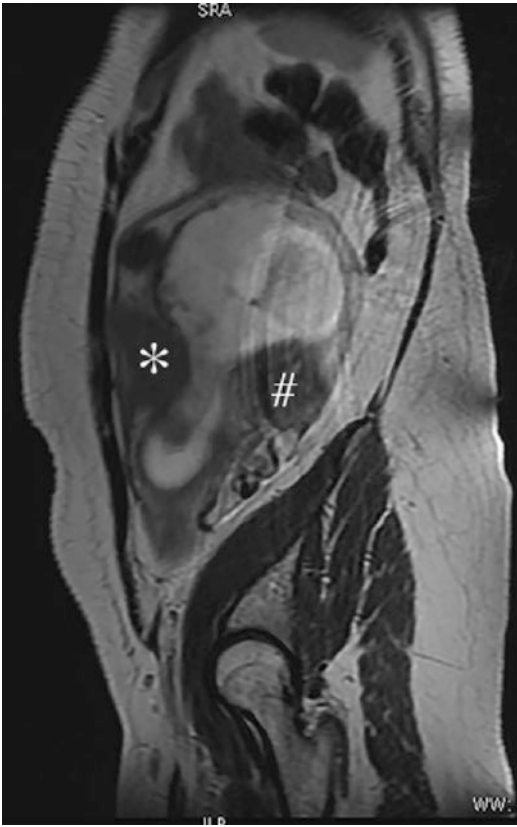
**Fig. 12.6** Ultrasound of degenerating uterine fibroid at the uterine fundus (marked with calipers). (Reproduced with permission from [77])

12.6.3 Abdominal MRI

Magnetic resonance imaging (MRI) evaluates uterine or adnexal masses (Fig. 12.7) when US is unequivocal. It was used preoperatively in 4.7% and exclusively postoperatively [24]. MRI also evaluates fetal status, the relation of the gestational sac to the pedicle of the UF (Fig. 12.8), and the relation of UF to other intra-abdominal structures. The findings mostly delineate compression of the colon, bladder, and proximal urethra (Fig. 12.9). MRI can demonstrate a hypointense vascular pedicle representing feeding vessels that arise from the uterine arteries, coursing from the uterus into an adjacent exophytic pelvic mass—*bridging vessel sign*. This sign reveals the uterine origin of the pelvic mass [78]. Postoperatively, MRI evaluates the myometrial thickness at the



**Fig. 12.7** T2-weighted MRI of a 12-week pregnant woman shows an 8 × 7 × 6 cm cystic and solid mass with septa. (a) sagittal view; (b) coronal view. (Reproduced with permission from [79] under the CC BY 3.0)



**Fig. 12.8** Three myomas of the anterior uterine wall. One is close to the uterine cavity and placenta implant area (\*). A posterior intramural myoma (#), with hyper-intense T2 weighted signal areas, is close to the posterior wall of the gestational sac, distorting it. (Reproduced with permission from [24])

site of the dissected peduncle [35]. Intra-abdominal bleeding from bleeding UF can be detected (Fig. 12.10). Also, MRI identifies the base of the cervical UF or defines the extent of concomitant endometriosis.

#### 12.6.4 Abdominal CT

Abdominal CT is used in an emergency after an inconclusive US, especially with suspected intra-abdominal bleeding [41] or when MRI is unavailable. CT use is common after delivery, revealing fast UF growth without free intra-abdominal bleeding [44]. UF complications are not a real emergency, and elective MRI use is common.



**Fig. 12.9** Abdominal MRI without contrast shows a 10 weeks gravid uterus with pregnancy in the fundus (star), compression of the colon (empty arrow), and compression of the urethra (filled arrow). (Reproduced with permission from [80] under the CC BY 2.0)



**Fig. 12.10** Fluid in the pouch of Douglas on abdominal MRI indicates intra-abdominal bleeding. Large subserosal myoma is above the gestational sac. (Reproduced with permission from [35] under the CC BY 2.0)



## 12.7 Treatment

*Operative management is contraindicated, for the symptoms subside with rest in bed, and further complications such as infection, are mostly unknown.*

(Wilfred Shaw)

*A myoma which rests in or on an impregnated uterus, does not of itself, demand the attention of the surgeon. Only when the tumor produces unpleasant symptoms is active interference indicated.*

(Theodore Landau, 1871 [81])

### 12.7.1 Historical Perspective

In the late nineteenth century, UF during pregnancy was treated depending on fetal viability. For viable fetuses, Cesarean section (CS), the Porro method, was performed [82]. Jules-Émile Péan, on December 15, 1874, made the first myomectomy [83]. John Knowsley Thornton, in 1879, performed the first unsuccessful myomectomy during pregnancy in England [84]. Later, Theodore Landau and Schröder published details of successful myomectomies. John B. Murphy, in 1896, unaware of the patient's pregnancy, made an abdominal hysterectomy for a large UF. When the uterus and UF were transected, he found a fetus of 3 months gestation and stated *Question of pregnancy had been thoroughly considered before operation, and thought impossible from the patient's statements and the absence of physical signs* [83]. In the same year, Richard Douglas made an abdominal hysterectomy at term with a stillborn [73]. Florence N. Boyd, in 1904, made two abdominal hysterectomies on the uterus with fibroids after CS with live births [85]. Victor Bonney reported the first successful Cesarean myomectomy in 1913 [86]. In 1920, William Mayo reported 19 myomectomies during pregnancy [87]. More than 100 operated cases have been published [14, 33, 35, 59, 80, 87–90].

### 12.7.2 Conservative Treatment

Despite often dramatic presentation, the optimal treatment for a degenerating UF is a short course of analgesics, bed rest, and reassurance. The pain will often improve dramatically, and the symptoms usually subside within 10 days [19]. The local release of prostaglandins from a degenerating UF can stimulate uterine contractions and premature labor.

Supportive care and administration of acetaminophen are suggested as the initial interventions (Grade 2C) [91]. A short course of opioids in standard doses or a 48 h course of nonsteroidal anti-inflammatory drugs (NSAIDs) can be given when initial measures do not control the pain. Pain may be managed with a short course of ibuprofen or indomethacin (25 mg orally every 6 h for 48 h) [91, 92]. NSAIDs should be limited to <32 weeks of gestation due to the possibility of inducing premature closure of the ductus arteriosus, neonatal pulmonary hypertension, oligohydramnios, and fetal/neonatal platelet dysfunction [93]. If NSAIDs are continued for >48 h, a weekly US assessment for oligohydramnios and narrowing of the fetal ductus arteriosus should be performed [91]. If either of these findings is noted, NSAIDs should be discontinued [91].

### 12.7.3 Operative Treatment

Only 2.6% of women with UF developed complications that required surgical intervention [14].

#### 12.7.3.1 Abdominal Access

Elective or emergent myomectomy is performed by laparoscopy or laparotomy, depending on the expertise, the degree of emergency and shock, and the need for simultaneous CS. Laparoscopy is mostly used for pedunculated UF [75]. Large UF, if not morcellated, are delivered through a small Pfannenstiel incision [75]. Laparotomy is still the preferred (87%), while 6.6% were operated on laparoscopically [24]. For the remaining operations, there are no data. The type of abdom-



inal incision is reported in only 6.5% [24]. For gasless laparoscopy, see Sect. 3.2.2.2.

### 12.7.3.2 Myomectomy

*For interstitial and subserosal fibroids  
No evidence supports recommending myomectomy during pregnancy in cases of obstetric disease, bleeding, necrobiosis, or threatened preterm delivery attributable to fibroids (Grade C).*

(French Guidelines 2012 [94])

### 12.7.3.3 Elective Myomectomy

*In the absence of data, a routine myomectomy after delivery is not indicated if a complication attributable to the fibroid occurred during pregnancy and the patient subsequently became asymptomatic again.*

(French Guidelines 2012 [94])

It is assumed that myomectomy should be avoided when entering the uterine cavity (the risk of damage to the amniotic sac cannot be excluded) or when a safe distance between the UF and the endometrial cavity cannot be assured [14]. An accurate preoperative assessment can improve the accuracy of surgical excision and reduce the risk of intraoperative complications. Management depends upon the: (1) location of the UF, (2) size and the number of the UF, (3) relation to the placenta, and (4) gestational age. Available options are as follows:

- Hysterectomy,
- Abortion with the removal of the tumor subsequently,
- Myomectomy with or without removing the fetus,
- The progress of pregnancy and solving emergencies if they arise.

### 12.7.3.4 Emergency Myomectomy

Myomectomy with the continuation of the pregnancy is indicated for the following conditions associated with UF as follows:

- Obstetric complications/fetal compression,

- Suspicion of other acute abdominal conditions requiring exploration,
- Twisted pedunculated UF,
- Bleeding UF,
- Uncontrollable pain or ruptured red degeneration UF,
- Rapidly growing tumor (intrafibroid bleeding or malignancy).

The most common indication of myomectomy in pregnancy is intractable pain [14]. Surgical intervention must be considered if symptoms persist after 72 h of therapy [92, 95].

Twisted pedunculated UF is untwisted first [75]. Subsequently, a linear cutting stapler is fired across the stalk of the pedunculated UF at the point of torsion. Some perform appendectomy [50]. The specimens are removed using a nylon extraction bag introduced through the left lateral trocar site, and the incision is extended (if needed) to remove the bag with its contents. The procedure ends with the staple line assessment for hemostasis (Fig. 12.11) with peritoneal irrigation.

Myomectomy for red degeneration is inevitable in 2% of cases [62]. Subserosal UF myomectomy or simultaneous CM should be performed by intracapsular technique and pseudocapsule sparing. UF pseudocapsule contains many neuropeptides and neurotransmitters. These substances



**Fig. 12.11** Staple line assessed for hemostasis after myomectomy at 10 weeks pregnancy. (Reproduced with permission from [50])

positively affect wound healing and improve subsequent sexual and reproductive functions [96]. Therefore, this technique minimizes the risk of uterine rupture during the same and further pregnancies (see Chap. 10). The augmented vascularization and tissue impedance of the pregnant uterus can amplify the risk of electrosurgical damage. Therefore, monopolar and bipolar electrosurgery in the UF resection should be avoided [97], although most UF enucleated laparoscopically were completed using bipolar diathermy [75]. Electrocautery and an argon beam coagulator to minimize blood loss show good results [98]. Some inject vasopressin into the capsule of UF to decrease operative blood loss [80]. After excision or extirpation, the defect should be closed with sutures and adequate hemostasis obtained. Rarely, cyst aspiration rather than myomectomy in a UF with cyst degeneration and pain can be performed [79].

In both forms of spontaneous bleeding, free subserosal UF bleeding into the abdominal cavity and intrafibroid bleeding resulting in fast-growing, very large UF, the uterine serosa is opened to identify the capsule of the UF before dissection of the peduncle. Then, the clamps are placed on the peduncle, and the myometrium is sutured with 1–0 resorptive sutures [35]. Although not recommended, free intra-abdominal bleeding can be stopped with sutures instead of a myomectomy [37].

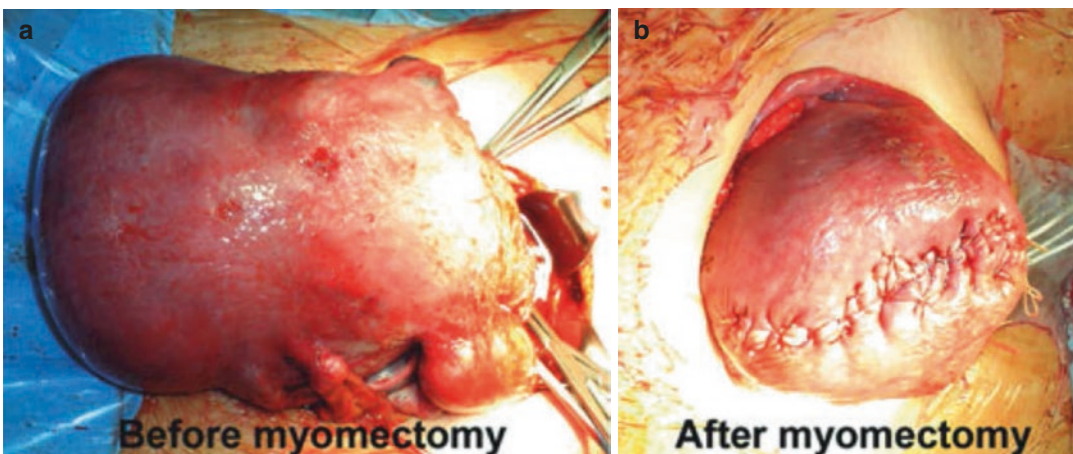
Acute urinary retention is due to (1) direct compression of the urinary bladder by UF or (2) UF causing uterine retroversion with resultant acute urinary retention (see Sect. 28.1).

### 12.7.3.5 Cesarean Myomectomy

*A myomectomy during a cesarean delivery does not seem to be associated with any more morbidity than short-term abstinence (LE3). Data on its long-term consequences are limited. There is no evidence to contraindicate myomectomy during a cesarean if it is either justified or necessary (pre-via) (grade C).*

(French Guidelines 2012 [94])

*Cesarean myomectomy* (CM) or myomectomy at the time of CS has been previously debated due to the risk of perioperative complications [99, 100], mainly bleeding [101]. Many advise against myomectomy at the time of CS [70], while others even advocate CM to minimize postoperative sepsis and postpartum hemorrhage [98]. Canadian guidelines support both antenatal myomectomy and CM [102]. The most recent meta-analysis did not show significant disadvantages compared to only CS. Compared to CS alone, an association exists between increased operative time and hemoglobin drop during CM. No increased rate of major bleeding or need for transfusion was identified [103]. CM (Fig. 12.12) should be carried out by senior obstetricians [95]. Indications for CM



**Fig. 12.12** Before and after Cesarean myomectomy [113]

with asymptomatic UF are [19, 95, 104] as follows:

- Single UF,
- Pedunculated UF,
- Subserosal UF,
- UF diameter  $\leq 75$  mm.

The optimal situation, with minimal complications, is CM of UF  $<5$  cm (or volume  $<50$  cm<sup>3</sup>) through the same uterine incision performed for the CS [105]. Subserosal or intramural UF are more common than submucosal when CM is performed [106–110]. CM is traditionally performed as *serosal intracapsular myomectomy* [110], referring to the excision of UF through the uterine serosa. With *endometrial myomectomy*, the UF is enucleated from the pseudocapsule, and the endometrium is sutured after UF removal [111]. This surgical technique minimizes adhesion formation on uterine serosa. The main advantage of CM is that UF can be easily excised because the UF pseudocapsule in a pregnant uterus is larger than that of a non-pregnant uterus, and the myometrium is more elastic and less delicate during pregnancy [112].

## 12.8 Prognosis

### 12.8.1 Maternal Outcome

#### 12.8.1.1 Maternal Mortality

The type of presentation and the type of treatment dictate the maternal outcome.

One of the first (fatal) cases of twisted pedunculated UF was in 1875 [48]. Until 1890, a preantiseptic era, maternal mortality was 22% [83].

Red degeneration does not lead to maternal mortality except with complications of spontaneous bleeding, which also does not add to maternal mortality.

Up to 1903, maternal mortality from bleeding UF was 75%, and no surgical treatment was attempted [33], and during the 50 years (1921–1972), it rapidly declined to 0% [33] and remained so until today [32–47].

#### 12.8.1.2 Maternal Morbidity

Obstetric complications of UF during pregnancy are out of the scope of this book. The risk of UF-related complications during pregnancy correlates with the size of the UF. UF  $>200$  cm<sup>3</sup> show a higher rate of complications than those  $\leq 100$  cm<sup>3</sup> [114]. The uterine wall localization (submucosal, intramural, or subserosal) may be responsible for specific adverse events. The retroplacental UF have a significantly higher risk of complications during pregnancy than other localizations [20, 68, 95]. The overall risk of CS from UF is more than double [115], up to 73% [19]. After myomectomy in pregnancy from any cause, CS is the mode of delivery in up to 94% [116].

The incidence of major complications with a CM is 29.5%, with intraoperative bleeding being the most frequent (27.3%) and commonly requiring a blood transfusion. Conversely, women with a CS alone (with a single UF) had a 15.7% rate of major complications, with intraoperative hemorrhage occurring in 13.7% of cases [104]. Uncontrollable bleeding during CM or isolated myomectomy in pregnancy can result in a higher rate of peripartum hysterectomy [19]. African studies did not find a difference in fetal outcomes between CM and CS with delayed myomectomy [106, 109].

The uterine rupture rate during pregnancy is increased with prepregnancy laparoscopic myomectomy. This can be minimized using intracapsular myomectomy (see Sect. 12.7.3.2).

Conservatively treated red degeneration does not result in preterm labor [19].

### 12.8.2 Fetal Outcome

Until 1890, the abortion rate was 40% [83]. Most fetal outcomes are referred from all types of presentations together. UF are associated with an elevated risk of fetal loss. The fetal loss rate is higher with multiple UF than with a single UF [117]. The pregnancy loss rate seems similar in surgically and conservatively treated patients [70, 116, 118, 119].

Fetal growth does not appear to be affected by the presence of UF [14, 120]. Rarely does large

UF compress and distort the intrauterine cavity. This leads to fetal deformities, including dolichocephaly (lateral compression of the fetal skull), torticollis (abnormal twisting of the neck), postural deformity, and limb reduction defects [121–124].

In the first half of the twentieth century, fetal mortality with bleeding UF was 29% [33], with sporadic fetal deaths during the following decades [38]. During the last 50 years, fetal mortality has been nil [33, 35–37, 41, 44–47].

Neonatal survival is excellent for elective myomectomy for painful or enlarging UF, from 92 to 97% [14]. African studies did not find a difference in fetal outcomes between patients undergoing CM with those undergoing CS with delayed myomectomy [106, 109].

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# Complicated Pelvic Inflammatory Disease

# 13

## Abstract

Pelvic inflammatory disease is rare during pregnancy. The most obvious reason is that many pregnancies are more or less desired, and one of the preparations is the prepregnancy treatment of any disease, especially of reproductive organs. Pregnancy is said to protect against pelvic infections, and clinicians are unlikely to suspect complicated pelvic inflammatory disease as a cause of an acute abdomen in pregnancy. The modern factor of pelvic inflammatory disease during pregnancy is assisted reproductive technology with the inoculation of infective pathogens to the peritoneal cavity. Therefore, techniques for preventing infection inoculation during assisted reproductive technologies are mandatory and discussed in detail. Clinical presentation is the same as in the nonpregnant population with the same differential diagnoses. Before the widespread use of abdominal sonography, preoperative or prelabor diagnosis was rare. Abdominal CT or MRI accurately defines the type and severity of the pelvic inflammatory disease. Accurate staging enables the use of the different therapeutic modalities available.

## 13.1 General Female Population

For an easier understanding of pelvic inflammatory disease (PID) characteristics in pregnancy, considerations in the general female population are presented.

### 13.1.1 Tubo-Ovarian Abscess

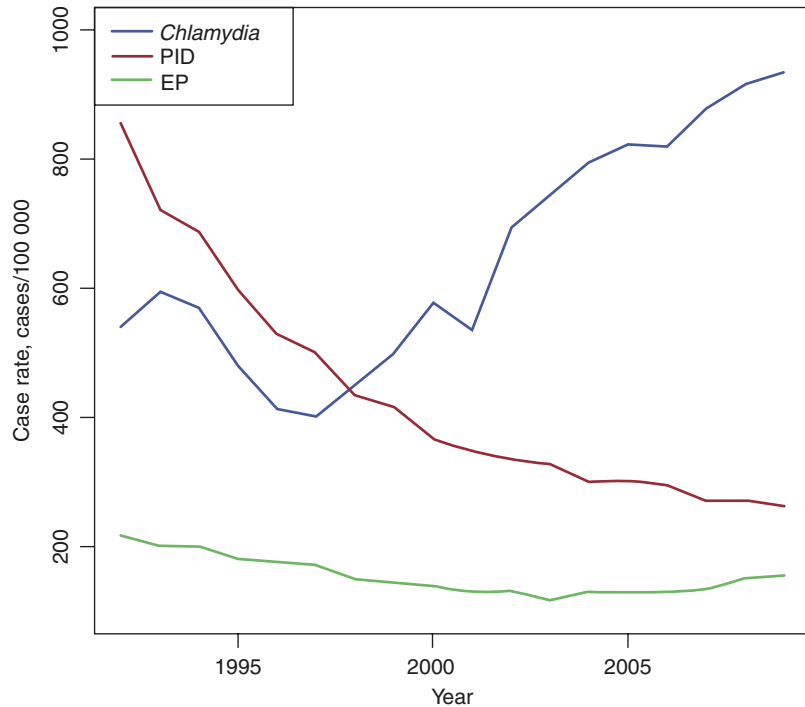
#### 13.1.1.1 Incidence

Despite increasing the number of broad-spectrum antibiotics, PID and its complications continued to reach epidemic proportions into the 1990s. Acute salpingitis and PID account for more than 350,000 hospital admissions and 150,000 surgical procedures per year [1]. Also, nearly one-third of patients hospitalized for PID develop some degree of pelvic abscess [2]. Other sequels such as ectopic pregnancy, salpingitis isthmica nodosa, tubal infertility, chronic pelvic pain syndromes, and pelvic adhesions are other consequences of PID (Fig. 13.1).

#### 13.1.1.2 Pathophysiology

A tubo-ovarian abscess (TOA) is the most severe manifestation of salpingitis. The intra-abdominal

**Fig. 13.1** Case rates for *Chlamydia trachomatis* infection (age, 15–39 years), pelvic inflammatory disease (age, 15–44 years), and ectopic pregnancy (age, 15–44 years), British Columbia, Canada, 1992–2009. *PID* pelvic inflammatory disease, *EP* ectopic pregnancy [3]



rupture of a TOA is potentially life-threatening, with mortality rates as high as 8.6% [4]. PID and subsequent TOA may result whenever bacteria access the upper female genital tract. Under normal circumstances, the fallopian tubes and related pelvic structures are sterile. However, access to the upper genital tract via sexually transmitted diseases or through instrumentation of the uterus may inoculate the uterus with bacteria from the vagina, causing infection. Passive transport and vectors, such as spermatozoa and *Trichomonas*, assist in the ascending infection from the polymicrobial vagina and cervix [5]. Once in sufficient numbers and virulence in the upper genital tract, these bacteria initiate an inflammatory reaction (endometritis–salpingitis–peritonitis) that results in the signs and symptoms of PID. The rate of a TOA developing from a typical PID ranges from 1–4% [6].

### 13.1.1.3 Microbiology

TOA is usually polymicrobial, whereas general pelvic infections may often be monomicrobial.

TOAs are usually a mixture of anaerobic, facultatively anaerobic, and aerobic organisms, with the purest isolated being anaerobes. The most frequent isolates from TOAs include a variety of *Enterobacteriaceae*, such as *E. coli* (37%), *B. fragilis* (22%), and other *Bacteroides* spp. (26%), *Peptostreptococcus* spp. (18%), and *Peptococcus* spp. (11%) [4, 7]. Sexually transmitted organisms such as *N. gonorrhoeae* and *C. trachomatis* are usually not present in the abscess but may be recovered from the cervix in one-third of cases. The emergence and recognition of *Prevotella bivia* (formerly *Bacteroides bivius*) and *Prevotella disiens* as major pathogens in upper female genital tract infection, combined with data suggesting that increased concentration of anaerobic organisms in the vagina is a risk factor for PID, point toward an anaerobic-predominant mixed infection as a cause of PID and TOA. These anaerobic bacteria, such as *Bacteroides* spp. and *Peptostreptococcus* spp., are commonly found in high concentrations in the vagina of women with bacterial vaginosis [5].

13.1.1.4 Prevention

Prevention of PID or prepregnancy treatment eliminates or minimized PID complications in pregnancy.

- Delay in the treatment of PID is associated with an increase in the risks of ectopic pregnancy and tubal factor infertility (LE3),
- Antibiotic therapy enables a cure in 80 to 90% of cases (LE1),
- Antibiotic treatment is indicated once the clinical diagnosis of PID is probable after microbiological samples are taken (grade A),
- Vaginal sampling for microbiological diagnosis is recommended before elective termination of pregnancy. (Pelvic inflammatory diseases: Updated French guidelines, 2020 [8]).

13.1.1.5 Clinical Presentation

The clinical diagnosis of TOA has similar diagnostic difficulties as PID. Women presenting with PID and pelvic mass may have a TOA, or it could be a hydrosalpinx, tubo-ovarian complex, or other complex adnexal mass. Patients with TOAs typically present with pelvic or abdominal pain and fever. A history of PID may be present in only 50% of patients. A significant proportion of women with TOA are afebrile (20–30%) (these have normal WBC counts) [2].

Pelvic examination usually reveals extreme pelvic tenderness (cervical motion tenderness), and mass may be present. If rupture has occurred, typical signs and symptoms of peritonitis are present and may lead to septic shock.

13.1.1.6 Diagnosis

Leukocytosis is common, but afebrile patients can have normal WBC levels [2]. CRP is a sensitive, specific inflammatory marker for predicting TOA in patients with complicated PID, and levels >50 mg/L suggest TOA [9].

Transvaginal ultrasound (US) is reliable for diagnosing and following conservatively managed TOAs [7]. A typical appearance is a complex or cystic adnexal mass with multiple internal echoes and septations. The “gold standard” for the diagnosis is laparoscopy. However, laparos-

**Table 13.1** Major and additive criteria for the diagnosis of PID

|                                                                                                                                                                                                                                                                                   |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Major criteria                                                                                                                                                                                                                                                                    |
| The absence of these criteria tends to rule out a PID diagnosis                                                                                                                                                                                                                   |
| Spontaneous pelvic pain (in the absence of another disorder) and                                                                                                                                                                                                                  |
| Induced adnexal pain and/or                                                                                                                                                                                                                                                       |
| Pain on uterine mobilization                                                                                                                                                                                                                                                      |
| Additive criteria                                                                                                                                                                                                                                                                 |
| Each of these criteria increases the probability of PID                                                                                                                                                                                                                           |
| History: Sexually transmitted infection; postpartum or postabortion; recent endouterine maneuvers; rectal syndrome (tenesmus, other anal spasms); vaginal bleeding                                                                                                                |
| Clinical examination: Temperature >38 °C; purulent leucorrhea                                                                                                                                                                                                                     |
| Laboratory tests: Elevated C-reactive protein; the presence of <i>chlamydia trachomatis</i> , <i>Neisseria gonorrhoeae</i> , or <i>mycoplasma genitalium</i> on bacteriological examination; endometritis on endometrial biopsy sample; salpingitis on the fimbrial biopsy sample |
| US: Thickening of the tubal wall (>5 mm); <i>cogwheel sign</i> (thickened tubal fringes resembling incomplete septa); heterogeneous latero-uterine mass potentially septated with fine echoes                                                                                     |

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PID pelvic inflammatory disease

copy may be reserved for uncertain diagnoses as US technology improves.

Criteria for PID in the general female population apply to the pregnant population (Table 13.1).

13.1.1.7 Treatment and Prognosis

Indications for surgery in the treatment of TOA are the same as in the nonpregnant population (see Sect. 13.9). CRP level trends correlate with the success or failure of conservative TOA management. Increasing CRP levels during treatment may be used as an indicator of the need for invasive intervention [9].

Intraperitoneal rupture of a TOA represents a true surgical emergency, but the extent of the surgery required to achieve a cure is controversial [7, 11]. Traditionally, aggressive surgery, usually total abdominal hysterectomy with bilateral salpingo-oophorectomy and drainage of all pockets of infection, was the treatment of choice. This radical approach was common because of the



**Table 13.2** Protocols for antibiotic therapy of uncomplicated PID in the general population

| Antibiotics                  | Dose and route           | Duration | Comments                                       |
|------------------------------|--------------------------|----------|------------------------------------------------|
| <i>First-line treatment</i>  |                          |          |                                                |
| Ofloxacin                    | 400 mg twice a day, oral | 14 days  | –                                              |
| Metronidazole                | 500 mg twice a day, oral | 14 days  | –                                              |
| Ceftriaxone <sup>a</sup>     | 500 mg im. Injection     | –        | –                                              |
| <i>Possible alternatives</i> |                          |          |                                                |
| Ceftriaxone <sup>b</sup>     | 500 mg im. Injection     | –        | –                                              |
| Azithromycin <sup>b</sup>    | 1 g per week             | 14 days  | Limited efficacy against anaerobes             |
| Moxifloxacin                 | 400 mg/day               | 14 days  | Higher cost; precautions for hepatic disorders |
| Ceftriaxone <sup>c</sup>     | 500 mg im. Injection     | –        | –                                              |
| Metronidazole <sup>c</sup>   | 500 mg twice a day, oral | 14 days  | –                                              |
| Doxycycline <sup>c</sup>     | 100 mg twice a day, oral | 14 days  | –                                              |

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<sup>a</sup> Can be used if necessary

<sup>b</sup> Used together

<sup>c</sup> Used together

inadequacies of antibiotics at that time. This procedure dropped the mortality rate from 100% to 12% [12] and could be the procedure of choice for a patient who has completed childbearing. In patients with severe complicated disease, total abdominal hysterectomy with bilateral adnexectomy may be necessary despite the patient's reproductive status. Patients without adnexa can still conceive via in vitro fertilization and embryo transfer (IVF-ET). Subtotal hysterectomy is another option [13]. Antibiotic therapy should include a broad-spectrum cephalosporin such as cefoxitin or cefotetan. Anaerobic coverage with clindamycin or metronidazole is mandatory, with their excellent ability to penetrate an abscess [7].

However, most women with a TOA are at the peak of their reproductive years, and fertility is a major issue. Conservative surgery should be attempted if the pathology is limited to one side and further reproduction is desired [14]. Conservative therapy of PID (Table 13.2) or an unruptured TOA (Table 13.3) consists of appropriate IV antibiotics [15], close monitoring of the patient, and possible drainage of the abscess via posterior colpotomy [15–17], CT- or US-guided percutaneous drainage, or drainage via laparoscopy. The posterior colpotomy approach has largely been abandoned because of a high complication rate. CT-guided percutaneous drainage success rates are in the range of 77–94% [18]. Early laparoscopic drainage with irrigation and antibiotics has a success rate of 95% [19].

**Table 13.3** Proposed IV antibiotic therapies of tubo-ovarian abscess in the general population<sup>a</sup>

| Substance <sup>b</sup>          | Dosage                   | Duration (days) <sup>c</sup> |
|---------------------------------|--------------------------|------------------------------|
| <i>First-line treatment</i>     |                          |                              |
| Ceftriaxone                     | 1–2 g once a day         | 14–21                        |
| Metronidazole <sup>d</sup>      | 500 mg three times a day | 14–21                        |
| + doxycycline <sup>d</sup>      | 100 mg twice a day       |                              |
| <i>Alternatives<sup>c</sup></i> |                          |                              |
| Ofloxacin <sup>d</sup>          | 400 mg twice a day       | 14–21                        |
| + metronidazole <sup>d</sup>    | 500 mg three times a day |                              |
| Cefoxitin                       | 1–2 g three times a day  | 14–21                        |
| + doxycycline <sup>d</sup>      | 100 mg twice a day       |                              |

Reproduced with permission from [10]

<sup>a</sup> In cases of septic shock, severe sepsis, or immunodepression, 3–8 mg/kg/d IV gentamicin can be added for no more than 5 days

<sup>b</sup> Reassessment of the antibiotic therapy at 72 h based on the clinical and microbiological results is essential. In the case of a de-escalation of the antibiotic spectrum, it is recommended that treatment against anaerobic microbes and *C. trachomatis* continue until the therapy is completed

<sup>c</sup> These protocols do not cover all bacteriological situations (e.g., the resistance of some gonococcal species to fluoroquinolones and the resistance of some enterobacteria species)

<sup>d</sup> Because oral bioavailability is good for ofloxacin, metronidazole, and doxycycline, it is possible to administer them orally as soon as the patient is no longer running a fever, has no gastrointestinal disorders, and has shown some clinical improvement

Drainage of a TOA in combination with antibiotic therapy is much more successful than conservative management. Patients treated with

antibiotics alone have a 50–70% success rate. The remaining patients eventually require surgical treatment [2, 5, 20]. Approximately 19% of conservatively treated patients require reoperation later [2, 20, 21]. Some advocate early surgical intervention for TOA, with the highest success rate (96.8%) and the lowest risk of readmission within 12 months (16.1%) [22]. Others recommend for patients above 40 years, febrile, and have a larger TOA, primary drainage at presentation [23]. In cases of grossly apparent bilateral disease, a somewhat conservative approach of bilateral partial adnexectomy without hysterectomy may be performed.

### 13.1.2 Ovarian Abscess

#### 13.1.2.1 Historical Perspective

William T. Black presented the first major series of 105 cases in 1936 [24]. *Streptococcus* spp. was found in 95%. The incidence of OA from all cases of PID was 6%, while other cited authors in that study claimed 12.4–15.45%. Wetchler and Dunn collected 120 cases in females until 1985 [25], and Stubblefield added five cases in 1991 [26].

#### 13.1.2.2 Pathophysiology

OA is a primary infection of the parenchyma of the ovary, an entity distinctly different from TOA. TOA, by contrast, involves the ovary by secondary spread from the infected fallopian tube [25]. Ascending infection is the most important mode of infection in nonpregnant women. OA has also been reported due to non-gynecologic conditions such as acute perforated appendicitis, colonic diverticulitis, distant infection from tonsillitis, typhoid, parotitis, and tuberculosis. Association of OA with an intrauterine device (IUD) has been noted, and some may be secondary to *Actinomyces* spp. [27, 28]. It may also occur due to a secondary infection in a dermoid cyst, serous cystadenoma, or a simple ovarian cyst.

## 13.2 Historical Considerations

In the sixth edition of *Antenatal and Postnatal Care*, Francis J. Browne, in 1946 [29], stated that salpingitis does not occur during pregnancy. Even in that era, and decades before this sixth edition, cases of PID during pregnancy were published [30–40]. Auguste (Marie Joseph Victor) Brindeau (Fig. 13.2) published the first cases in 1917. He reported a case of fatal peritonitis from OA rupture immediately after a term delivery [42]. In addition to 12 personal cases of salpingo-oophoritis during pregnancy, Brindeau collected 81 more cases. Of these, 44 were operated on [35]. Up to 1939, he added 23 personal cases [35]. These cases, not described in detail, were reported as being of an “unprecise nature.” In many, if not all, the etiology was implied to be criminal interference. Aleck W. Bourne, in 1921, made detailed pathophysiology and progression of acute puerperal salpingitis [43]. French gynecologists also added to this subject at that time—Auvray in 1925 [39], Fruhinsholz, Hamant, and Mosinger in 1929 [44], Devraigne and Ravina in 1937 [45], Bidoire in 1939 [34], and Metzger in 1939 [46]. Their cases occurred about the second month of pregnancy, sometimes earlier, and were almost invariably diagnosed as ectopic pregnancy or acute appendicitis.

Lauchlan Aitken, in 1870, made the first description of a ruptured primary ovarian abscess (OA) during premature labor in the seventh month of pregnancy, with fetal and maternal death [47]. Then HC Coe, in 1891, described three cases. One had an OA rupture into the urinary bladder and later delivered a viable infant [48]. KH Öhman, in 1913, operated on 7 days after an uneventful delivery due to acute pelvic symptoms with a mass to one side, which proved to be a streptococci pyo-ovarium [40]. Tenani, in 1921, reported the rupture of a pyo-ovarium during the second stage of labor [49]. Pomini, in 1939, described a ruptured OA on the fifth day following a rapid, uneventful delivery [50].



**Fig. 13.2** Auguste (Marie Joseph Victor) Brindeau, a French gynecologist (1867–1955), worked in Paris, finally at the *Clinique Tarnier*, where he retired. One of the

founding members of the journal *Gynécologie et Obstétrique* in 1919. (Reproduced with permission from [41]; webpage Biusanté Paris)

### 13.3 Incidence

#### 13.3.1 Acute Salpingitis

Acute salpingitis in pregnancy is rare. Metzger, in 1939, made a 15-year review of French literature and found only seven references [46]. Up to 1959, all reported cases (12 cases) occurred in the first half of pregnancy [51]. Recent cases confirmed salpingitis as early as the peri-implantation period [52]. Acute salpingitis is more common during the first trimester [53]. The average mean gestational age for PID is 19 weeks [54]. It probably occurs earlier but is diagnosed during the second trimester.

#### 13.3.2 Tubo-Ovarian Abscess

PID, in the form of a pelvic and peritoneal abscess, rarely complicates pregnancy for several reasons. First, in cases of a wanted pregnancy, future mothers live healthy life avoiding any risks, including sexually transmitted diseases.

Second, women with “gynecological problems” visit gynecologists more often to eliminate any possibility of interfering with a future pregnancy. Diseases during the prepregnancy period are cured, minimizing the possibility of disease flare during pregnancy. Third, women during gestation use protection more often. Fourth, the cervical mucus plug and intact amniotic membrane protect against ascending infection.

Acute salpingo-oophoritis or pelvic abscess mainly occur early after transvaginal oocyte retrieval (TVOR) [55] or in the first trimester [56, 57] and is almost always on the right side [58, 59]. There is no side predilection in IVF-ET because TOA starts on the side of TVOR. Up to 2021, at least 44 cases of TOA were published [60–67]. Pelvic infection readily occurs or presents in the puerperium if there is an infection of the birth canal during or following parturition [61]. Pelvic infection after TVOR for IVF-ET is <0.6% [68–71]. A pelvic abscess develops in <50% of these cases [69]. Up to 1959, 20 cases were collected, with bilateral TOA present in 50% of cases [51].

### 13.3.3 Ovarian Abscess

Although the true incidence of OA in pregnancy is unknown, it seems it is extremely rare [25, 27, 40, 47–49, 51, 72–81]. According to Dudley et al., the ratio of OA to TOA is increased in pregnancy [58].

### 13.3.4 Intramyometrial and Uterine Horn Abscess

These entities are not described as part of PID, but it is mentioned here due to the same possible etiological factors. These are the rarest entities, with only one report for both intramyometrial (two cases) [82] and uterine horn abscess [83] found.

## 13.4 Etiopathogenesis

*The extension of the inflammation by simple contiguity from the pelvic to the abdominal peritoneum is especially liable to occur in cases of puerperal pelvi-peritonitis at about the end of the second week when the patient has not taken sufficient care of herself.*

(Gustave Bernutz)

*Sometimes a pus tube forms after conception has occurred, the woman having been infected and impregnated at the same time.*

(Joseph Bolivar Delee, 1938 [84])

### 13.4.1 Suppurative Salpingitis

#### 13.4.1.1 Acute Suppurative Puerperal Salpingitis

Aleck W. Bourne, in 1921 described acute puerperal salpingitis, which differs in many aspects from that of non-puerperal origin [43]. By the end of the first week, when symptoms manifest, the fallopian tubes lie at or just above the pelvic brim near the iliac vessels. At the same time, the ovaries are placed below, just within the pelvis, and applied to its lateral walls. The former is, therefore, outside the limitation of the pelvic basin, surrounded by coils of the small intestine; this considerably alters

the results which will follow the escape of pus from the abdominal ostia, as compared with a similar tubal condition in which the tubes are lodged within the pelvic cavity. In the latter case, the resulting abscesses are strictly circumscribed in the pouch of Douglas, and the whole inflammatory area tends to be roofed in and delimited by the omentum or small intestine. The general extension of the infection into the abdominal peritoneum is unusual, and the symptoms and signs are correspondingly localized. Resolution is a frequent result; the patient recovers without operation and may regain a fair state of health. However, conditions differ in puerperal salpingitis. The abdominal location of the tubes is the cause of abdominal, not pelvic peritonitis, since it allows the outpouring of pus among the coils of the small intestine at or just above the level of the sacroiliac joint, and herein lies the essential difference between the two varieties of salpingitis. This difference manifests as much in the physical signs exhibited as in the treatment required. Further, the hyperthermic condition of the uterus and appendages during the puerperium will also modify the gravity of the symptoms and the rapidity of their course.

The involution of the uterus appears to be arrested at a point at which the fundus extends about halfway between the symphysis and the umbilicus. This may be due to infection within its cavity or possibly to a neighboring active suppuration in the tubes. However, the important result is that the tubes are maintained at their high level at or above the pelvic brim for a considerable time after the inception of the disease. Moreover, the large uterus nearly fills the pelvic cavity and affords a fixed point comparatively high up in the abdomen, proper for developing adhesions with other parts.

In the acute stage, the tubes are greatly congested and edematous, especially the ampullary portion, while the fimbriae are protruding, and the ostium is discharging pus. The isthmus may appear quite normal or swollen to a lesser extent. Any adhesions at first are light and easily separated, often due to flakes of recent lymph and chiefly involving adjacent coils of the small intestine and part of the cecum or sigmoid colon.

The abdominal ostium frequently opens into a small abscess cavity walled in by the adherent coils

and situated at first just in front of and above the sacroiliac joint. Later, when suppuration has extended, it tends to pass forward along the brim of the pelvis toward the uterine corn and is shut in from above by the greater omentum, or the pus may even come into relation with the abdominal wall.

#### 13.4.1.2 Acute Salpingitis

A risk factor for acute salpingitis is an ectopic pregnancy or vice versa. Coues of Boston, in 1911, reported 214 ectopic pregnancies with 16% of mild catarrhal salpingitis in the opposite fallopian tube. Other etiopathogenetic factors are the same as in TOA (see Sect. 13.4.2).

### 13.4.2 Tubo-Ovarian Abscess

During pregnancy, pelvic infection occurs independently of the gravid state, or the infection may exist before the pregnancy. Friedman and Bobrow have proposed four mechanisms for OA or TOA during pregnancy [51] as follows:

- Hematogenous spread as in pelvic tuberculosis,
- Lymphatic spread, especially from the vagina and cervix,
- Infection of a (previously) existing ovarian cyst,
- A flare-up of an old infection.

Metzger described similar mechanisms in 1939 [36] as follows:

- Infection at the time of fertilization,
- Infection soon after fertilization before the uterine cavity has become closed by conception (12 weeks),
- Vascular or lymphatic spread (from a septic focus in the vagina or cervix),
- A flare-up of preexisting infection,
- Instrumentation sufficient to overcome natural barriers,
- Ascending infection associated with threatened abortion and intrauterine bleeding.

When infection occurs during fertilization, attachment and detachment of gonococci to human sperm occur. The gonococcus acts as a “hitchhiker” on the traveling sperm until a favorable environment for detachment is encountered, such as in the uterus or fallopian tube [85]. Different pathogens have susceptibility to specific routes of infection and its spread. Gonorrheal PID is often bilateral by ascending infection, while tuberculosis PID results from hematogenous infection [51].

#### 13.4.2.1 In Vitro Fertilization–Embryo Transfer

TOA is a rare complication of TVOR, which usually fails. It occurs in 0.2–0.5% of TVOR [68, 86], but 32% of all OA were after TVOR [60]. Three different pathways for inoculation are described [70, 87, 88] as follows:

- Inoculation of vaginal microorganisms and anaerobe opportunists by puncture through the non-sterile vagina,
- Reinfection through puncture of chronically infected ovaries,
- Infection through direct bowel puncture with an inflammatory or infectious spillage.

Techniques to decrease the risk of pelvic infection include [86, 89–92] the following:

- The fewest possible vaginal punctures (2 max.),
- Vaginal preparation (0.5% saline or 10% povidone-iodine),
- Prophylactic antibiotics (IV cefazolin).

Prophylactic antibiotics following TVOR are controversial as pelvic inflammation is uncommon, and these medications may not prevent all associated infections. Antibiotic prophylaxis is recommended in groups with a higher risk for infection (see Sects. 13.4.2.2 and 13.4.2.3).



### 13.4.2.2 In Vitro Fertilization–Embryo Transfer and Endometriosis

Endometriosis/endometrioma is a risk factor for PID and TOA/OA development following TVOR [64, 66, 93–95]. Up to 80% of PID following TVOR had underlying endometriosis [69]. Among its risk factors, incidental aspiration of an ovarian endometrioma during TVOR activates the pelvic infection [93, 96, 97]. Old blood in endometrioma provides a culture medium for bacteria to grow slowly after transvaginal inoculation. This explains the role of endometriosis in predisposing patients to PID [93]. Endometriotic pseudocapsule and old blood inside may prevent antibiotic prophylaxis from overcoming the transvaginal bacterial inoculation [93]. Furthermore, the altered immune system of a patient with endometriosis might fail to overcome the inoculated bacteria [69].

Previous reports had indicated that aspiration of endometriotic cysts before ovulation induction for ART resulted in a better clinical outcome [98]. To prevent infection in patients with endometrioma undergoing TVOR, the endometrioma should be aspirated before TVOR [99]. However, these endometriotic cysts reexpand quickly after aspiration, and it is difficult to harvest some oocytes without puncturing through these chocolate cysts. In addition, the chocolate content of the follicular fluid is sometimes found incidentally after aspiration [100]. Endometriosis surgery does not affect ART outcomes and does not increase unresponsiveness to ovarian stimulation [101]. Moreover, the ovarian reserve may be adversely affected by the surgical excision of endometrioma [102].

Endometriosis is a risk factor for developing a TOA or an OA [95]. Infection-preventing measures should be applied not only before and immediately after TVOR. The excision of endometrioma less than <4 cm in diameter is discouraged before ART [103, 104].

### 13.4.2.3 Previous Pelvic Inflammatory Disease

The risk of infection is higher in cases of previous PID [70, 88, 105–107]. Unilateral TOA may be explained by a “flare-up” of preexisting but latent salpingitis [108]. This possibility would seem to necessitate a low-grade infection of the fallopian tube in the first instance leaving sufficient patency to permit the passage of a fertilized ovum. After nidation, the infection may become acute, probably because of the congestion produced by the gestation or unilateral salpingitis, the other fallopian tube being patent and functioning [109]. Another proof of a “flare-up” of the previous infection is an intraoperative finding of adhesions between the loops of the intestine, the uterus, and the tubo-ovarian tissue indicating the chronic nature of the disease [110].

Pelvic actinomycosis is considered a genuine, albeit exceedingly rare, hazard of IUD. In one study from the general female population, all 12 cases of OA were associated with IUD use, and some were of actinomycotic origin [25]. As an IUD-related pregnancy complication, ovarian actinomycosis is even more exceptional, and a history of IUD is common [27, 28]. The IUD colonizes the endometrium, from where the bacteria proceed through the tube and into the peritoneal cavity, eventually gaining access to the ovarian substance at ovulation. Why actinomycotic involvement of the fallopian tube sometimes does not occur is unclear unless the dissemination of *A. israelii* is blood-borne or lymphatic rather than the result of ascending infection.

During the first half of the twentieth century, tuberculous salpingitis with intrauterine pregnancy was more frequent [111]. The frequency with which pregnancy occurs in the presence of pelvic tuberculosis is difficult to assess for the following reasons: (1) The incidence of unsuspected pelvic tuberculosis in apparently healthy females is unknown; (2) pelvic tuberculosis may be discovered after pregnancy has occurred; (3) in proved cases of pelvic tuberculosis, pregnancy has rarely been reported.

### 13.4.2.4 Puerperium

Puerperium appears to be the least likely time to develop a TOA because ascending infection, the major pathophysiology in developing PID in most women rarely occurs during this phase. The co-existence of vaginal colonization and delivery has been associated with severe infections, such as endometritis, salpingitis, and TOA [112]. Vaginal *S. pneumoniae* colonization was present during CS. Neither the antenatal amoxicillin for group B *Streptococcus* prophylaxis nor intraoperative prophylaxis with cefazolin prevented maternal and neonatal infection [113]. In 1870, Lauchlan Aitken made a different statement: “*That suppuration is more common in the puerperal than in any other variety of pelvic inflammation – whether in the serous membrane or cellular tissue – is a fact disputed by no one; and I think it also probable, that not only is suppuration much the most common termination in such cases, but also that the matter forms much more rapidly*” [114]. One explanation could be that TOA started during pregnancy but was diagnosed in the puerperium.

### 13.4.2.5 Tubal Sterilization

The incidence of TOA is minimal because the procedure blocks communication between the genital tract and the pelvic cavity [115]. Theoretically, this blockage should prevent an ascending transmission of any organisms, if present, from the genital tract proximal to the site of tubal sterilization into the peritoneal cavity. This is supported by clinical evidence that complete or even partial tubal occlusion appears to lessen the severity of infection [115]. Three possible explanations of TOA after previously occluded tubes have been proposed [115] as follows:

- Persistent tract or reconnection between the two tubal segments,
- Factors related to the operative procedure,
- Systemic factors such as a hematogenous or lymphatic bacterial spread with an immunocompromised state.

Time intervals from tubal occlusion to TOA range widely, from as early as 36 h to 12 years [115].

### 13.4.2.6 Genital Anomalies

Structural genital anomalies are risk factors for pelvic abscess during pregnancy [56, 106, 116]. It is unknown whether (1) anomalies themselves or (2) invasive procedures directed to correct these anomalies or to enable pregnancy are the real cause/risk factor of the pelvic abscess.

### 13.4.2.7 Infective Non-Gynecologic Etiology

The etiologies may include infective non-gynecologic conditions such as ruptured colonic or Meckel’s diverticulitis or acute appendicitis (Table 13.4). It is specified whether the abdominal operation itself is a risk factor [56, 106] or operation due to intra-abdominal infective cause such as TOA results in infective complication [117]. Even TOA of unknown origin has been reported [14].

## 13.4.3 Ovarian Abscess

An OA is a primary infection of the ovary without the involvement of the fallopian tube, whereas a TOA involves both the fallopian tube and the ovary.

The ratio of ovarian to tubo-ovarian abscess increases in pregnancy [58].

The possible factors for OA include the disruption of the ovarian capsule, giving bacteria access to the ovarian stroma, and hematogenous

**Table 13.4** Differential diagnoses of pelvic inflammatory disease in pregnancy

| Gynecologic/obstetric   | Non-gynecologic         |
|-------------------------|-------------------------|
| Ectopic pregnancy       | Perityphlitic abscess   |
| Threatened abortion     | Acute appendicitis      |
| Endometrioma            | Meckel’s diverticulitis |
| Adnexal torsion         | Colonic diverticulitis  |
| Hemorrhagic cyst        | Urinary tract infection |
| Ovarian hematoma        | Iliopsoas abscess       |
| Ovarian vein thrombosis | Crohn’s disease         |
| Placental abruption     | Urolithiasis            |
| Chorioamnionitis        |                         |
| Pelvic neoplasm         |                         |
| Uterine horn abscess    |                         |

and lymphatic spread [25]. Nevertheless, the most common mechanism is an alteration of the ovarian capsule at ovulation or penetration during surgery or surgical procedures. Patients with OA commonly have a history of salpingitis, endometriosis, pelvic adhesions, hydrosalpinx, or pelvic surgery [70, 93].

The interval between capsule disruption and clinical presentation varies depending on the bacterial load, type of bacterium, its virulence, and whether the infection occurred secondary to direct contamination at surgery, or spread through devitalized tissue, most commonly after vaginal hysterectomy, ovarian cystectomy, CS, during pregnancy, the use of an IUD [25, 118], or transvaginal/percutaneous needle aspiration of an endometrioma [96, 119]. Nevertheless, despite the advantages of image-guided vaginal oocyte collection, there are inherent risks, such as injury to blood vessels and hemoperitoneum, trauma to pelvic organs, infection or exacerbation of PID, rupture of endometriotic cysts, ureteral lesions, and hyperstimulation [71, 120–122].

OA after TVOR or transcervical ET occurs in 0.2–2.2% [68, 70, 71, 123]. Risk factors include (1) ovarian or pelvic endometrioma (most common) [87, 94, 96, 105], with old blood providing a rich culture medium for bacterial proliferation [88], (2) previous (operated or non-operated) ectopic pregnancy [124, 125], and 3) follicle aspiration even without any subtle pelvic pathology [71].

The etiology of OA in pregnancy is uncertain and different from that in the nonpregnant state. Ascending infection is the most important mode of infection in nonpregnant women. Barriers to ascending infection in pregnancy include cervical mucus plug, intact fetal membranes, and the decidua covering the openings of the fallopian tubes. Several classifications and mechanisms [51, 126] are proposed for infection of ovaries during pregnancy (see Sect. 13.4.2). Data confirming these facts are that OA readily occurs in the puerperium if there is an infection of the birth canal during or following parturition. Also, it is likely that the ovary becomes infected independently of the gravid state or that the infection exists before the pregnancy. During the last

decades, the more common cause is TVOR as a part of IVF pregnancy (see Sect. 13.4.2.1) [73, 94, 127].

### 13.4.4 Intramyometrial Abscess

The etiology of this exceptionally rare abscess location (two cases) failed to reveal a cause [82].

## 13.5 Microbiology

The most common isolate was *N. gonorrhoeae* [54]. Bacterial confirmation of pelvic infection is rarely available after transvaginal punctures, including *E. coli* [128] and subclinical infection with *C. trachomatis* [129], and rare isolate in general population *Atopobium vaginae* [130], *S. aureus*, and mixed anaerobic bacteria [94]. Anaerobic opportunists of the vagina are found with pelvic abscesses after TVOR. *E. coli*, *B. fragilis*, *Enterococcus* spp., and *Peptococcus* spp. are common [70, 71]. There are also case reports with other microorganisms, such as *Fusobacterium necrophorum*, during puerperium [131]. TOAs are usually polymicrobial. Organisms isolated from TOAs belong to the facultative anaerobe Enterobacteriaceae family (*E. coli*, *Proteus* spp., *Klebsiella* spp.) and anaerobic *Peptostreptococcus* spp., *Streptococcus* spp. or *Actinomyces* spp. in nonpregnant women [27, 106, 108, 132, 133].

During the first half of the twentieth century, tuberculous salpingitis with intrauterine pregnancy was more frequent [111]. Today, these are rare.

## 13.6 Clinical Presentation

### 13.6.1 Suppurative Salpingitis

#### 13.6.1.1 Acute Suppurative Puerperal Salpingitis

Aleck W. Bourne described the clinical presentation of all stages of acute puerperal salpingitis in 1921 [43]. It differs in many aspects from that of

non-puerperal origin. Essentially, the tubes are abdominal and not pelvic organs, which are usually affected before reaching their normal positions in the pelvic cavity. Like acute appendicitis, pain precedes everything and is rapidly followed by a slowly rising temperature becoming 38.9–39.4 °C on the third or fourth day, with a pulse the following suit. Vomiting is not a feature in early cases. Occasional, indicative symptom consists of retention of urine or painful micturition. This is common when cellulitis develops secondarily to the salpingitis involving the upper part of the broad ligament and extending forward beneath the round ligament around the bladder. Without operative treatment, fever is persistent with chronic pain and wasting.

In the early stages, the abdomen is not rigid. There is nothing but tenderness accurately localized to a point about 2 in. below and external to the umbilicus, i.e., over the posterior part of the lateral brim of the pelvis. The uterine fundus rises about 5 cm above the symphysis. It may or may not be tender at first, but later it becomes so, especially if adhesions become attached to the uterine corn or secondary cellulitis develops.

After a week or more, finding a mass in the hypogastrium to one side of the uterine fundus is not unusual. Except for cellulitis, which is felt immediately above Poupart's ligament, such a tumor is nearly always due to adherent omentum and coils of the distended gut. Later, as suppuration spreads, there is rigidity and tenderness of the whole hypogastrium, with extension upwards over the ovarian veins if these vessels have thrombosis.

By way of the vagina, the signs are difficult to appreciate, for the primary changes are not in the pelvis, and the gentlest manipulation causes pain. The uterus can feel enlarged, with limited mobility soon developing and complete fixity. In the first few days, it is symmetrically in the pelvis. However, later it may be displaced laterally by secondary cellulitis, and the displacement is toward the affected side.

During the first week, there may be little or nothing felt in the lateral fornices. However, later an indefinite tender mass can be felt very high up in the posterolateral region, largely made up of

the ovary surrounded by adherent coils enclosing pus. The accessible part of Douglas' pouch seldom, if ever, contains anything by the vagina. The posterior portion of the lower part of the uterine body may give the impression of a tumor because it tends to bulge backward immediately above the cervix. The best palpation of the pelvis is obtained by rectal examination. High up on one or both sides, the early composite swelling can be made out early, becoming larger and more distinct as time passes.

A swelling high up in the broad ligament disturbing the position of the uterus is probably a mass of secondary cellulitis.

### 13.6.2 Tubo-Ovarian Abscess

Pregnancy is said to protect against pelvic infections. Clinicians are unlikely to suspect a pelvic abscess as a cause of an acute abdomen in pregnancy. A detailed history should search for [27, 72] the following:

- Previous episodes of PID,
- Unexplained spontaneous abortions,
- Intrauterine device.

The clinical presentation between ruptured and unruptured TOA differs. In unruptured cases, the first signs of the disease are sometimes mild and not specific, and the findings may be altered significantly by the size of the gravid uterus [56, 93]. The time of symptom onset is highly variable, ranging from 5 days to 287 days of gestation [60]. Recurrent abdominal or pelvic pain symptoms in the postoperative and interpregnancy periods suggest the chronic nature of the disease. However, the courses of antibiotics and the low virulence of the organisms result in chronic pelvic infection. History of pelvic pain can be present for several months or years [13]. A history of PID is present in only 50% of patients. The infection may flare up and present at any time during pregnancy. Pain is mostly gradual in onset, but it finally has become so severe that the patient cannot be out of bed. While at rest, intermittent cramping, like menstrual cramps, could

be present. There are no gastrointestinal symptoms [13]. There is no vaginal bleeding, and the membranes are intact, but cervical discharge is often present [116], especially with gonorrheal cervicitis [126]. Patients with TOAs typically present with pelvic or abdominal pain and fever. A significant proportion of women with TOA is afebrile [13] (many of these have normal WBC counts) [2].

Classic clinical presentation of TOA is abdominal pain, cervical motion tenderness, and adnexal tenderness, as well as one of the following:

- Fever  $>38^{\circ}\text{C}$  ( $101^{\circ}\text{F}$ ),
- Abnormal cervical discharge,
- Elevated ESR or CRP or positive cervical cultures for *N. gonorrhea* or *C. trachomatis*.

The abdominal examination can reveal a suprapubic or low abdominal mass. It can be mildly tender with cystic consistency. Vaginal tenderness during palpation of the fornix is elicited on the side of abdominal pain [31]. If no classical clinical features of acute peritoneal or pelvic infection are present, it is mostly not suspected preoperatively and can be found only during emergent or elective CS [134]. In ruptured cases, peritonitis results in pyrexia and sometimes vomiting [14].

With localized TOA, pelvic mass can be found. It could be a hydrosalpinx, tubo-ovarian complex, or other complex adnexal mass. Ruptured TOA results in generalized tenderness over the entire uterus. The uterus is very irritable, and minimal stimulation produces contractions. Abdominal wall guarding on the side of the rupture is present.

If rupture has occurred, peritonitis may lead to septic shock. Pelvic examination usually reveals extreme pelvic tenderness (cervical motion tenderness), and mass may be present. The cervix is closed if there are no signs of preterm labor. The vaginal examination can reveal evidence of a pre-

vious gonorrheal infection, such as the swelling of Bartholin's orifices and granulation of the vaginal mucosa [30].

A pelvic infection becomes clinically evident within hours up to a few days after TVOR. The time from TVOR to the manifestation of a frank pelvic abscess is highly variable. Diagnosis of PID after IVT-ET mainly occurs within the first week after the procedure [68–70, 93] and in  $<25$  days in 50% [73]; however, there are cases with symptoms even postpartum [107]. PID after IVT-ET with underlying endometriosis has the same symptoms and signs, including cervical and adnexal tenderness, the rise of body temperature to  $>37.8^{\circ}\text{C}$  for 48 h, cervical discharge, WBC count  $>12,000/\mu\text{L}$ , and elevated ESR.

### 13.6.3 Ovarian Abscess

Clinical presentation depends on whether the abscess is unruptured or ruptured. Women with OA during pregnancy may present a wide range of clinical symptoms with an unruptured abscess. Presentation depends on the type of the bacteria, the load of the bacteria, whether the infection is mono- or polymicrobial, and the patient's immune status. Most cases (with or without subsequent pregnancy) present with indolent onset of abdominal or pelvic pain [87]. The interval between TVOR and symptom onset is generally short but highly variable and occasionally prolonged (mean, 38.5 days; median, 22.5 days; range, 1–320 days) [87]. If pregnancy follows TVOR, OA develops within 4 weeks in 50% of patients and the remaining 50% from 4 weeks to the postpartum period [87]. (Low-grade) fever is present in 95% of patients [73, 87] but could be the only symptom in 50%.

Detailed history reveals the risk factors for TOA (see Sect. 13.6.2). Palpable mass can be detected. On speculum examination, the cervix and vagina are healthy. In cases with impending rupture, diffuse lower abdominal pain may worsen to severe pain associated with anorexia, nausea, and vomiting in case of rupture. A woman with a ruptured OA presents with features of diffuse peritonitis [27].



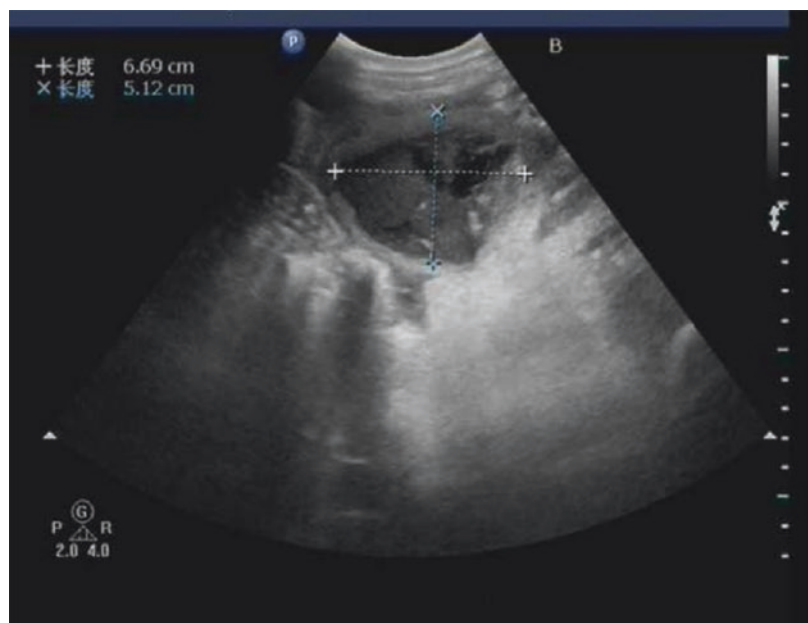
## 13.7 Differential Diagnosis

Table 13.4 summarizes gynecologic and non-gynecologic causes of inflammatory conditions in the pelvic region and lower abdomen. Differential diagnosis is somewhat different between early (ectopic pregnancy, threatened abortion) and advanced (placental abruption, chorioamnionitis, ovarian vein thrombosis) pregnancy (see Sect. 15.6). Sometimes, it is difficult to differentiate between types of PID, such as TOA and uterine horn abscess. The most common differential diagnoses are acute appendicitis/perityphlitic abscess and ectopic pregnancy [37, 54]. Sigmoid diverticulitis should be excluded with left lower quadrant abdominal pain [135, 136].

## 13.8 Diagnosis

Before the widespread use of US, preoperative or prelabor diagnosis was rare. English literature of 19 cases until 1977 found that the diagnosis was made preoperatively in only one case (5.3%) [106]. In most cases, the diagnosis was made during emergent CS when complicated PID causes fetal distress, preterm labor, or preterm premature rupture of membranes [134] or symptoms and signs of acute abdomen.

**Fig. 13.3** Transvaginal sonography of a solid and cystic mass (6.7 cm × 5.6 cm × 5.1 cm) with an irregular contour in the left adnexal region at 31 weeks of IVF pregnancy. (Reproduced with permission from [60])



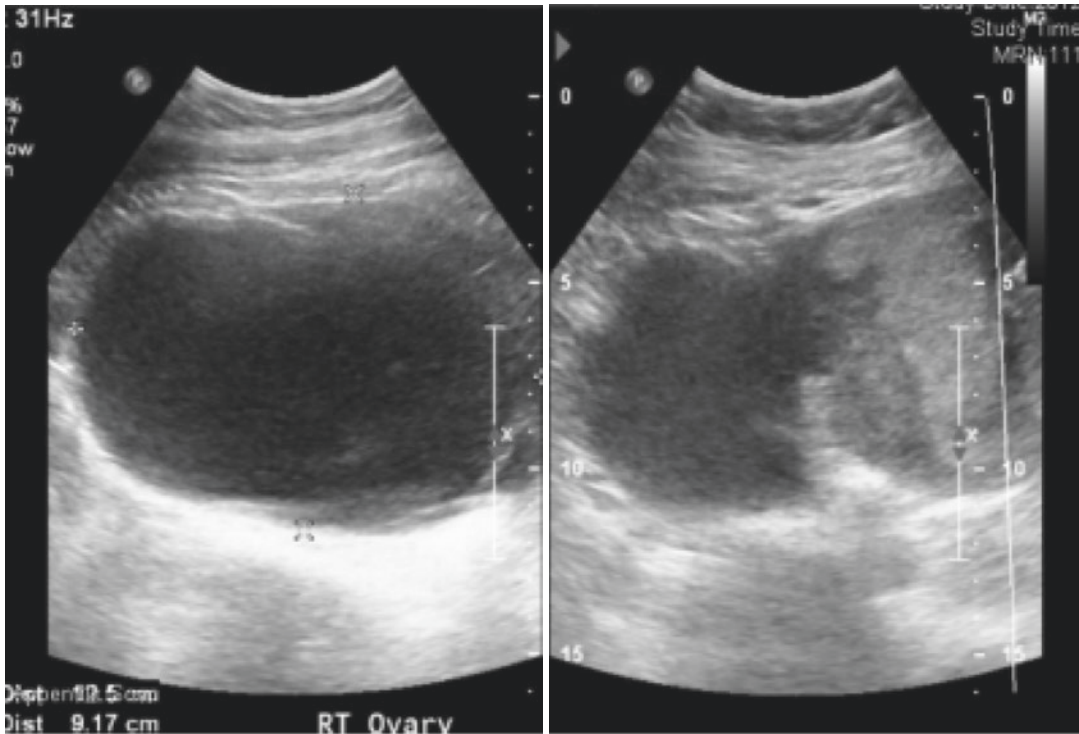
### 13.8.1 Laboratory Findings

Leukocytosis is a prerequisite of OA, and the ESR and CRP are elevated [73, 87]. A Papanicolaou smear is a simple and effective method for diagnosing uterine actinomycosis in pregnancy [28]. Distinguishing from adnexal tumors can be difficult for a localized disease on imaging, and CA 125 is not tumor-specific (see Sect. 8.4.1).

### 13.8.2 Abdominal Ultrasound

Abdominal US should be the first diagnostic imaging modality for suspected PID [15, 137]. Transvaginal sonography (TVUS) allows detailed visualization of the uterus and adnexa, including the ovaries. The fallopian tubes are usually visible only when abnormal and distended, primarily from postinflammatory obstruction. Common TVUS characteristics of TOA are large, solid, and cystic mass with an irregular contour in the adnexal region. Free fluid in the cul-de-sac indicated ruptured PID (Fig. 13.3).

Transabdominal sonography (TAUS) is less sensitive in late gestation when an enlarged uterus interferes with adequate compression of the abdominal wall with the probe. TAUS is complementary to the TVUS because it provides a



**Fig. 13.4** Transabdominal sonography of a 12.5 cm right ovarian cyst in pregnancy. (Reproduced with permission from [138] under the CC Attribution License)

more global view of the pelvic contents (Fig. 13.4), whether TAUS (bladder filling required) or TVUS (bladder filling not required) is performed first and whether the complementary examination is needed for a final diagnosis [137, 139].

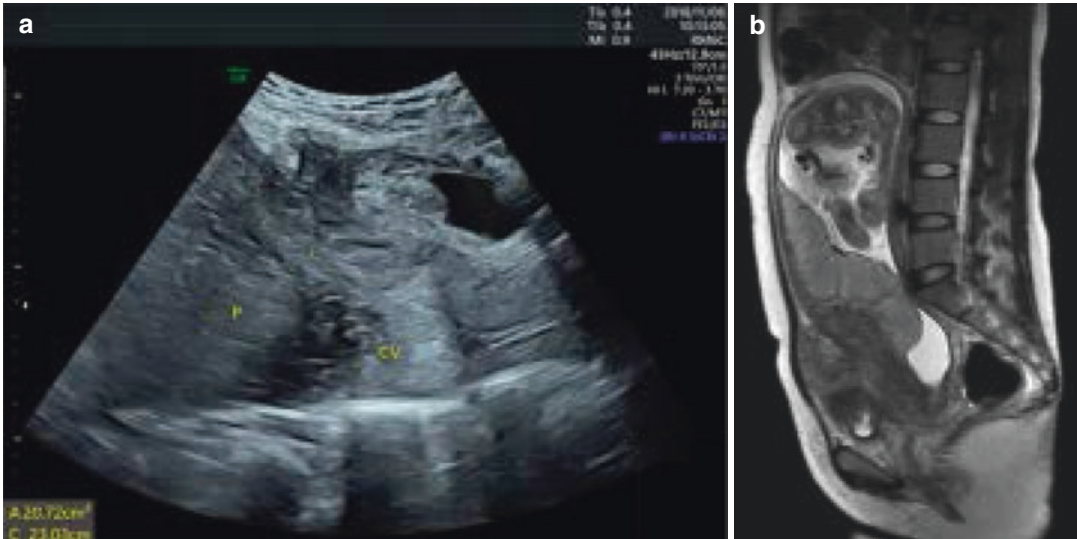
Serial TAUS can detect mass enlargement, presumptive of TOA [66, 107]. Free intra-abdominal fluid has a high probability of ruptured TOA. The sensitivity of US for the diagnosis of TOA is 56–93%, with a specificity of 86–98% [139]. The wide range is likely due to variability in the technology used (TAUS vs. TVUS), the person performing and interpreting the US (radiologist vs. gynecologist), the study population (patients with suspected PID and patients with a palpable adnexal mass and suspected PID vs. only patients eventually requiring laparoscopy or surgery in the workup of their PID), the study design (retrospective vs. prospective), and interpretation of positive

results (inclusion of any adnexal mass vs. limiting it to those diagnosed explicitly as an abscess) [139]. TAUS is excellent for the follow-up of percutaneous or conservative treatment [62].

Pyosalpinx is a thick-wall cystic “sausage”-shaped structure with an incomplete septum. Pelvic actinomycosis from IUD shows a space-occupying lesion in the lower abdomen, affecting the bladder, lower uterine segment, and upper segment of the cervix (Fig. 13.5a).

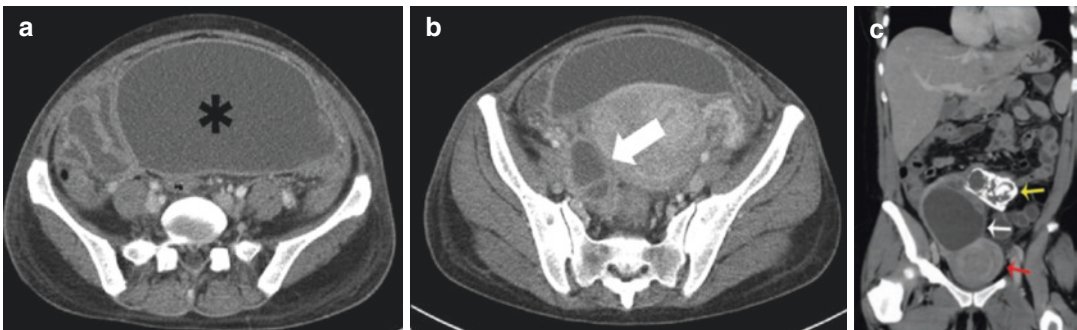
### 13.8.3 Abdominal CT

For these indications, an abdominal CT scan is avoided during pregnancy. However, if MRI is unavailable or during the postpartum period, CT is used for suspected TOA (Fig. 13.6a, b) or associated pathologies such as ectopic pregnancy (Fig. 13.6c).



**Fig. 13.5** Diagnosis of pelvic actinomyces. (a) A space-occupying pelvic cavity lesion on US affected the bladder and the lower uterine segment wall. (b) Penetrating

placental implantation with bleeding was suspected on MRI. (Reproduced with permission from [28])



**Fig. 13.6** Abdominal CT. (a, b) Pelvic abscess (asterisk) and right tubo-ovarian abscess (arrow) at 19 weeks of gestation. (c) Coronal view of the fetal skeleton (yellow

arrow), tubo-ovarian abscess (white arrow), and leiomyomatous uterus (red arrow) [140]. (Reproduced with permission from [141])

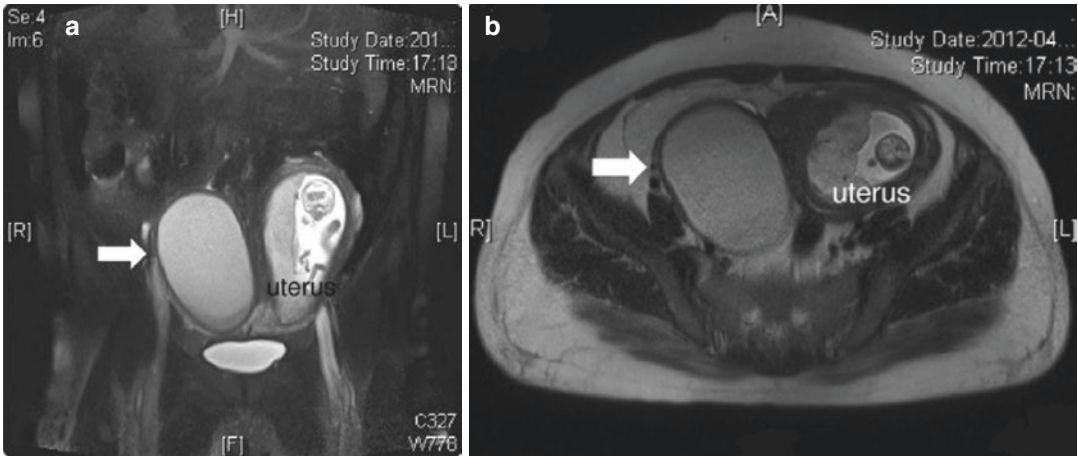
### 13.8.4 Abdominal MRI

Abdominal MRI is indicated when US findings are equivocal (Fig. 13.7). Abdominal MRI is more accurate than TAUS in diagnosing PID in the general female population. The sensitivity is 95%, the specificity 89%, and the accuracy 93%. For TVUS, the corresponding values are 81%, 78%, and 80% [142]. In pregnant patients, abdominal MRI reveals or confirms cystic mass with septations [107, 138]. Abscess or mass around the lower pole of the uterus and cervix is

suspicious of actinomyces, especially with a history of IUD (Fig. 13.5b). The additional benefit is an exclusion of acute appendicitis with right-sided mass [107].

### 13.8.5 Bacterial Cultures

In the general female population with acute PID, one-third of the cultures from culdocentesis and fallopian tube exudates are sterile [143–145]. The explanation is recurrent salpingitis, which



**Fig. 13.7** (a, b) Pelvic MRI shows an  $11.5 \times 6.7 \times 9.0$  cm right-sided ovarian cyst with internal loculation (white arrow) and an intrauterine pregnancy. (Reproduced with permission from [107])

destroys the tubal architecture obstructing the passage of the organisms into the peritoneum and intracellular organisms (e.g., *Chlamydia* spp.), not isolated from exudates. Improper culture techniques for viruses, *Chlamydia* spp., etc., cause falsely sterile cultures.

The positive endocervical culture for *N. gonorrhoeae* stresses a relatively high frequency (6%) of asymptomatic gonorrheal infection in pregnancy [145].

On initial evaluation with suspected or proven (pyo)salpingitis, routine endocervical cultures should be obtained in all pregnant patients.

## 13.9 Prevention

### 13.9.1 Preprocedural Elimination of Endometriosis

Endometriosis predisposes to TVOR-induced PID (see Sect 13.4.2.1 and 13.4.2.2). Complete evaluation and removal of endometrioma should be considered [105]. With endometriosis and pelvic adhesions, non-vaginal methods of oocyte

recovery, like the transabdominal approach, seem preferable.

### 13.9.2 Procedural Vaginal Antisepsis

Traditionally, the vagina is not prepared with antiseptic solutions (e.g., aqueous povidone-iodine) before TVOR since these agents are considered embryotoxic. Therefore, only normal saline irrigation of the vagina is usually the norm before TVOR. However, most believe that using only normal saline rinsing and irrigating the vagina canal can wash away the vaginal discharge without destroying potentially harmful bacteria preexisting in the vaginal flora. An additional antiseptic solution followed by a normal saline solution can eliminate most or entire vaginal flora. This process would not jeopardize the development of the oocyte because all the antiseptic solution has been completely flushed away before TVOR [100].

Vaginal preparation with povidone-iodine or chlorhexidine solution compared to saline or not cleansing immediately before CS probably reduces the risk of post-cesarean endometritis [Level of evidence MODERATE] [146].



### 13.9.3 Prophylactic Antibiotics/ Antifungal Agents

Older studies question prophylactic antibiotic use, given the low incidence of pelvic infections [86, 92, 123]. Others, however, do advocate using prophylactic antibiotics [71, 89, 90]. Although there is no consensus on the type and protocol for antibiotic use, doxycycline and metronidazole are most commonly used. First-generation cephalosporins, routinely used as prophylactic antibiotics preoperatively, are also used before TVOR [87]. Due to several *C. glabrata* infections diagnosed in the second half of gestation following IVF, some recommend fluconazole, an antifungal agent, as part of the protocol before TVOR [89, 147].

Another approach is antibiotic prophylactic in high-risk patients, such as those with a history of PID or endometriosis. Patients with OAs almost always have a history of salpingitis, endometriosis, pelvic adhesions, hydrosalpinx, or pelvic surgery [70, 71]. Prophylactic antibiotics during TVOR are recommended in these groups of patients with increased risk [70, 93].

## 13.10 Treatment

### 13.10.1 Medical Treatment

The most frequently used antibiotic before 1970 was penicillin. After 1985, gentamicin and clindamycin were most commonly used [54]. There are insufficient data from clinical trials to recommend a specific regimen for pregnant women with PID, and empirical therapy with agents effective against *N. gonorrhoeae*, *C. trachomatis*, and anaerobic infections should be considered. Local antibiotic sensitivity patterns should be taken into account (e.g., IV ceftriaxone 2 g once daily plus IV erythromycin 50 mg/kg once daily, with the addition of metronidazole given orally [500 mg twice daily], per rectum [1 g three times daily], or IV [500 mg three times daily]) (Evidence level III, B) [148]. Prolonged antibiotic therapy is probably necessary for infected endometrioma. Therapy should be

guided not simply on clinical improvement but on infected endometrioma culture and sensitivities and achievement of effective concentrations of the drug at the site of infection [149].

#### 13.10.1.1 Tubo-Ovarian Abscess

A *minor* pelvic infection (0.3% of cases) is defined by pyrexia and pelvic tenderness with no evidence of abscess formation on US. Early infection can be treated with antibiotic therapy [15, 70]. More severe infections leading to TOA also occur in 0.3% [68, 70]. Unruptured pelvic abscess or TOA may be given supportive care and treated by preoperative broad-spectrum IV antibiotics effective against gram-positive, gram-negative, and anaerobic bacteria for at least 72 h before operative intervention. There are no guidelines addressing earlier operative intervention after ART, and the possible worse outcome has not been documented. Unsuccessful prolonged antibiotic treatment could carry a high rate of spontaneous abortion [62].

#### 13.10.1.2 Ovarian Abscess

The optimal management of TVOR-related OA during pregnancy is unclear. Ruptured OA with peritonitis requires urgent surgical intervention. Whether drainage should be delayed in more stable clinical settings is uncertain. IV antibiotics effective against gram-positive, gram-negative, and anaerobic bacteria should be administered.

The easier spread of infection is present in advanced pregnancy when ovaries are out of the pelvis.

### 13.10.2 Nonsurgical Drainage

For unruptured TOA, under US or CT control, percutaneous [56, 150] or transvaginal catheter drainage combined with IV antibiotics is suggested as the first-line treatment to prevent postoperative complications because that procedure is minimally invasive and easy to perform [55,



59, 60, 107]. Peristaltic bowel on US helps avoid bowel puncture.

Percutaneous US-guided drainage during pregnancy has a 40% failure rate [60]. This is due to small-diameter catheters or multiloculated abscesses, resulting in incomplete abscess drainage. Drainage failure could result if delivery occurs before the complete drainage of the abscess. The catheter might dislodge from the abscess during delivery or postpartum uterine involution when the ovary is drawn back into the pelvis.

TOA after TVOR can be treated with TVUS-guided drainage with posterior colpotomy and T-drain replacement into the cul-de-sac. The elimination of infection resulted in term delivery [55].

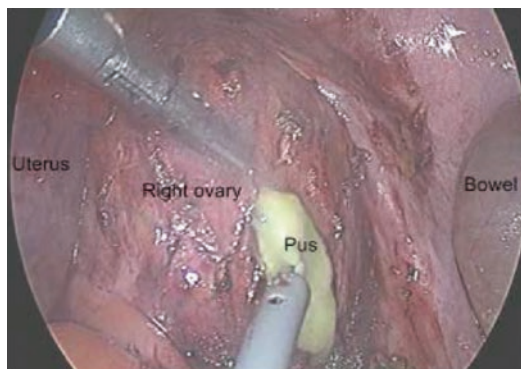
### 13.10.3 Surgical Treatment

Two-thirds underwent exploratory laparotomies, one-third underwent unilateral salpingo-oophorectomies, and a quarter underwent appendectomies [54].

#### 13.10.3.1 Indications

Surgical treatment was performed in 88% of pregnant patients with TOA [105], indicating that surgical intervention is usually necessary. In the general female population, US TOA morphology cannot predict the necessity for operative treatment [151]. Indications for surgical therapy for both TOA and OA include [67, 152] the following:

- No response to antibiotics within 72 h,
- Abscess rupture or adjacent organ rupture,
- Surrounding organs affected by the inflamed mass,
- Unsuccessful drainage of the abscess,
- Uncooperative patient for percutaneous drainage,
- Uncertain diagnosis.



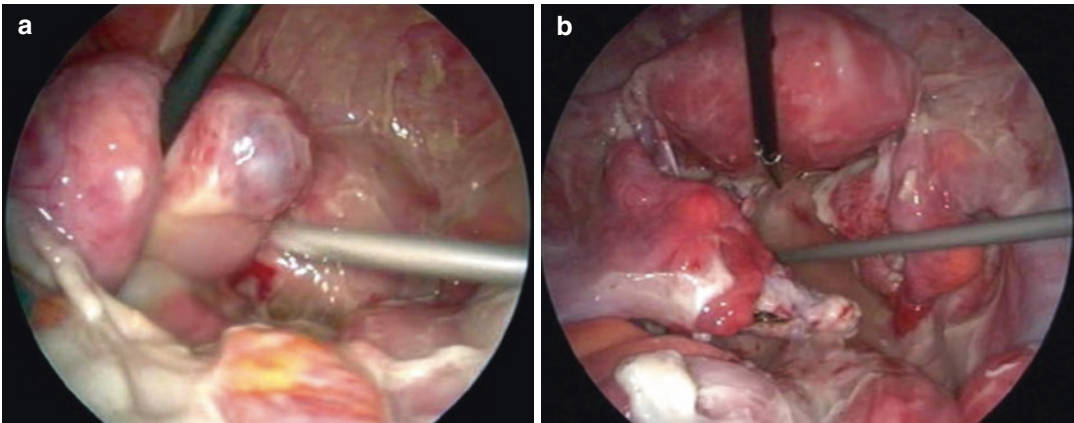
**Fig. 13.8** Laparoscopic image of ovarian cyst. A 10-cm right-sided ovarian cyst with pus made severe adhesions with surrounding pelvic organs and peritoneum. It also contained an endometriotic lesion. (Reproduced with permission from [138])

#### 13.10.3.2 Operative Principles

Most patients are young, and conservative surgery should be attempted if the pathology is limited to one adnexa [14].

Surgical drainage with postoperative antibiotics should be the first-line therapy, albeit there is no consensus on management [87, 153]. Apart from nonoperative drainage (see Sect 13.10.2), operative peritoneal lavage with drainage is common by laparoscopy [73, 81, 112, 138]. If severe pelvic adhesions secondary to abscess formation prevent completion of the laparoscopic procedure, the conversion to laparotomy is indicated. For non-urgent conditions, the second trimester of pregnancy has classically been considered the safest period for surgical intervention.

An aspiration or abscess drainage (Fig. 13.8) has a failure rate of 37.5%, while resection of the abscess (Fig. 13.9) has only 4.3% [60]. In cases with large unilateral adnexal masses, especially when ruptured, isolated resection of the fallopian tube [31], unilateral salpingo-oophorectomy [66, 110, 152, 153], or even hysterectomy with unilateral or bilateral salpingo-oophorectomy, especially during postpartum could be done [120, 131]. Hysterectomies are more common among multiparas [131, 154]. Pregnant women with unilateral involvement managed by preserving the contralateral ovary and the tube have a favorable outcome [13, 14, 75, 106, 132, 155].



**Fig. 13.9** (a) Laparoscopic image of a left ovarian mass consistent with abscess and disseminated purulent fluid. (b) Appearance after excision of the mass and irrigation of the pelvis. (Reproduced with permission from [73] under the CC BY 2.5)

#### 13.10.4 Obstetric Management

CS is the most common mode of delivery [54]. With late decelerations, fetal bradycardia, or an increase in uterine contractions of a viable fetus, CS is performed during operative treatment of ruptured PID [60]. In near-term pregnancy, induction of labor is recommended. When the fetus is removed from the source of infection, any antibiotic can be administered to the mother. Also, if conservative therapy fails, laparoscopy is technically easier with the smaller uterus in the postpartum period [156].

### 13.11 Prognosis

#### 13.11.1 Maternal Outcome

##### 13.11.1.1 Tubo-Ovarian Abscess

At the beginning of the twentieth century, maternal survival was excellent, with more cases of pelvic tuberculosis during pregnancy [157]. With completely changed underlying microbial flora causing complicated PID in pregnancy, the maternal outcome is still excellent, with survival approaching 100% [73, 158]. Delay in diagnosis and treatment, especially with ruptured TOA causing peritonitis, increases the possibility of maternal mortality and morbidity [56]. Fertility impairment following TOA results from postinflammatory tubal obstruction [159].

Compared to non-PID patients, PID patients have approximately 2× higher risk of preterm labor and ectopic pregnancy [160].

Due to a small number of patients and various PID stages, firm conclusions cannot be made. Surgical and percutaneous intervention carries 50% of the spontaneous abortion rate in first-trimester pregnancies. The TOA caused by TVOR seems to be better maintained during pregnancy, and the perinatal outcome is better than the naturally occurring TOA [67]. Surgical and percutaneous intervention could have a similar 50% abortion rate during the first trimester. During 14–20 weeks of pregnancy, the cases are exceptionally rare, and conclusions cannot be made. After 20 weeks of gestation, surgical treatment has a high delivery rate but cannot be compared to other methods performed in 1–3 patients [67]. Spontaneous TOA and TOA after TVOR have similar ratios (3:1) of delivery and abortion after 20 weeks of gestation. Through all trimesters, TOA without therapy has a 100% abortion rate [67].

##### 13.11.1.2 Ovarian Abscess

Tenani, in 1921, reported the rupture of a pyo-ovarium during the second stage of labor, followed by maternal streptococci peritonitis and death [49]. Currently, maternal survival is 100% [27, 72]. Pelvic actinomycosis has low virulence, which is probably why spontaneous abortion

does not occur. The preterm labor rate could be increased, but the number of cases is too small for definitive conclusions [27, 28].

### 13.11.1.3 Surgical Complications

Surgical complications influence further pregnancy and delivery, including surgical site infections, increased intra-abdominal pressure, and burst abdomen (see Chap. 22) [152].

## 13.11.2 Fetal Outcome

Fetal and neonatal mortality combined is 10.3–50% [54, 161, 162]. The majority of births are at term [54]. Term delivery results from surgical [133, 163] or antibiotic [164] treatment during pregnancy. Live births have a high incidence of associated morbidities, such as neurological sequelae [161, 162]. Neonates can develop early- or late-onset sepsis and often have no apparent perinatal risk factor [162]. Reasons for the increase of pneumococcal neonatal sepsis recently may be the following: (1) increased rates of genital *S. pneumoniae* colonization due to changes in sexual practice (i.e., increased orogenital sex); (2) improved laboratory isolation techniques; (3) the increased use of antimicrobials for prevention of group B streptococcal disease selecting for more resistant pathogens such as *S. pneumoniae* [165]; and (4) publication bias with positive cases being published more frequently [161]. Possibly the type of bacteria dictates the rate of fetal loss (spontaneous abortion). The most common is type II atrial septal defect (Or 4.2) [166].

Acute PID in pregnancy results in an increased rate of congenital cardiovascular anomalies (OR 2.6).

Up to 1971, gonorrheal salpingitis/TOA had 50% fetal loss [126].

Fruhinsolz and Feuillade, in 1924, in their classical paper dealing with utero-adnexal tuberculosis and pregnancy, referred to cases reported by various observers of normal pregnancy following conservative surgery for pelvic tuberculosis [157]. Today, pelvic tuberculosis in pregnancy is extremely rare.

### 13.11.2.1 Acute Salpingitis

Previously, the fetal outcome was poor. Up to 1993, the average gestational age at diagnosis was 12 weeks; 27% of patients reached term pregnancy and delivered; 40% resulted in spontaneous abortions, 13% in stillbirth, and 7% in premature delivery with fetal death [167].

### 13.11.2.2 Tubo-Ovarian Abscess

Several possible explanations for the role of infection in reducing pregnancy success have been suggested, especially during IVF-ET pregnancy with PID. Introducing endotoxin-releasing bacteria into the peritoneal cavity during TVOR may induce abortion by promoting the release of prostaglandins, catecholamines, and cortisol, which play a role in the termination of pregnancy. Moreover, local inflammatory reactions and fever may also affect pregnancy success rates [168].

Overall fetal loss was 36.8%, and surgically treated patients included 92.9% of overall fetal loss [60]. Pregnancy loss occurred in 90%, with TOA developing before 24 weeks of gestation [105]. The fetal survival rate of those pregnancies complicated by a TOA late in the second trimester was 33% [106, 169]. The fetal mortality rate after PID from IVF-ET depends on the gestational age and reaches 40–50% overall [107, 138]. A full-term pregnancy is reached in 1/3 of cases [107].

### 13.11.2.3 Ovarian Abscess

Fetal mortality from OA depends on many factors. Different authors claim different survival. Some claim extremely low fetal survival, with live cases delivered prematurely with severe fetal complications [56, 73, 87]. Others claim excellent survival of healthy newborns [27, 72].

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**Abstract**

Vernix caseosa (VC) peritonitis is an extremely rare, poorly recognized complication caused by an inflammatory response to amniotic fluid spilled into the maternal peritoneal cavity. Two classic forms are recognized: VC peritonitis and VC granuloma. The third form is meconium peritonitis/granuloma. Meconium, apart from detritus and digestive tract secretions, also contains ingested amnion with lanugo hair. With fetal distress, the fetal intestine empties. VC complications present during the first postpartum days with abdominal pain and pyrexia. Nausea, vomiting, and dyspnea due to diaphragmatic irritation are common. Contrast-enhanced abdominal CT reveals multiple oval rim-enhancing peritoneal lesions commonly misinterpreted. Nonoperative treatment includes antibiotics and steroids with a low success rate. Surgical treatment includes

lavage with the removal of all masses. Incorrect preoperative diagnosis results in removing many intra-abdominal organs commonly attributed to malignancy. Maternal survival is excellent, but the sequel is common with operative and nonoperative treatment.

**14.1 Definition and Historical Perspective**

*Vernix caseosa peritonitis* (VCP) is an extremely rare, poorly recognized complication caused by an inflammatory response to amniotic fluid spilled into the maternal peritoneal cavity. The term *vernix caseosa* (VC) first appeared in 1846 in the Dunglison Dictionary of Medical Sciences. The first description of the term VCP was by Martin S. Krumerman and Gerald J. Pouliot in 1976 after the Cesarean section (CS) [1]. It was an unreported complication before the era of CS.

## 14.2 Incidence

Less than 40 cases of VCP have been reported to date [2–6]. However, the incidence of VCP is undoubtedly underestimated because many cases with mild symptoms likely go unnoticed.

## 14.3 Pathology

### 14.3.1 Physiology of Vernix Caseosa

Birth is a state of rapid transition from the high-humidity aqueous intrauterine environment to the characteristically low-humidity (typically 20–40%) extrauterine environment. VC is the cheese-like substance covering the skin of the newborn, unique to humans during the last trimester of pregnancy, unique to humans. This material in the amniotic fluid consists of an admixture of (1) fetal desquamated, anucleate, squamous, epithelial cells, (2) lanugo hair shafts, and (3) sebaceous glandular secretion. Biochemical studies have revealed the presence of lipids (62.5%), proteins (36%), and carbohydrates (1.5%) [7]. After delivery, VC dries spontaneously on the skin. VC has multiple protective functions such as moisturizer, anti-infective, antioxidant, and enhancer of the acid mantle development after birth [8]. VC undergoes a substantial change during birth and is transferred from an aqueous, warm, and sterile environment to a gaseous, colder, and xenobiotic-containing environment postnatally [9]. Differences exist in VC composition between newborn boys and girls. Higher proportions of wax esters and triacylglycerols with longer hydrocarbon chains were observed in newborn girls [10]. The gestational age was likely to affect branched-chain fatty acids concentrations, with the VC and meconium branched-chain fatty acids content being significantly higher in full-term infants than in preterm infants [11]. VC is more prominent following CS than after vaginal births [12]. VC is absent in very low birth weight premature infants [8].

### 14.3.2 Vernix Caseosa Peritonitis/Granuloma

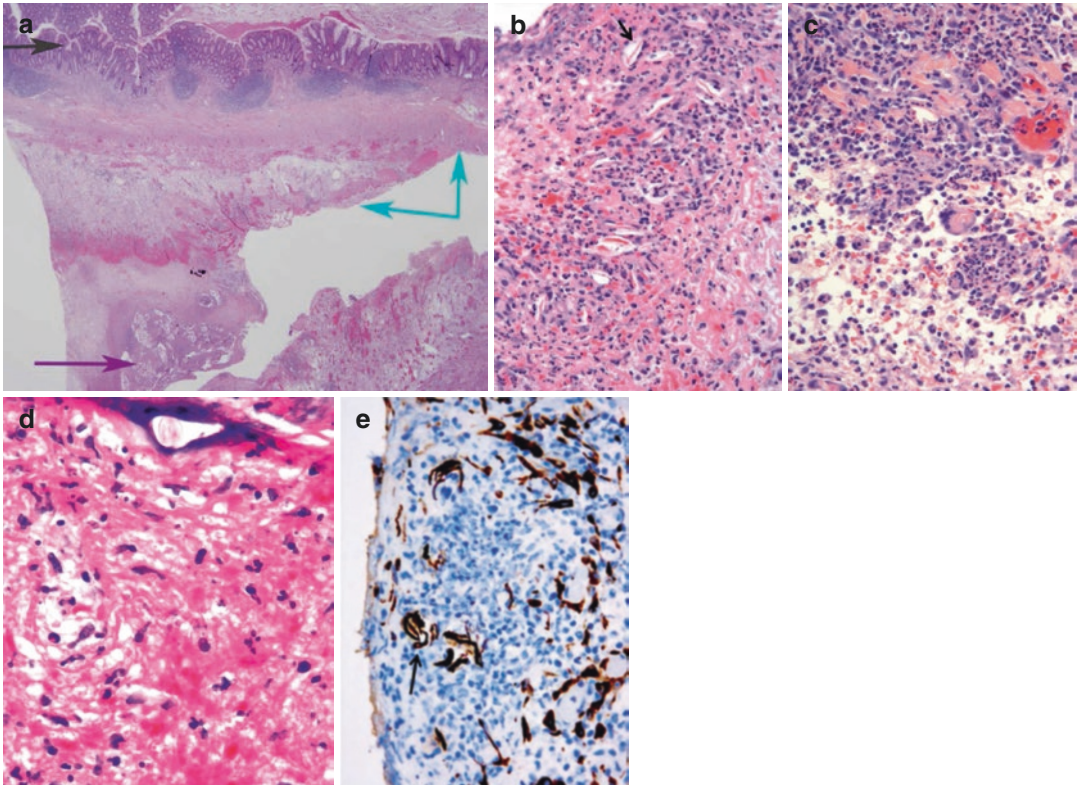
(Unawareness of) VC commonly results in appendectomy. Only microscopic examination demonstrates multiple fibrinocellular exudates on the appendiceal serosa (Fig. 14.1a). The inflammatory cells include an admixture of neutrophils, eosinophils, lymphocytes, and macrophages aggregated about anucleate squamous cells having wrinkled borders (Fig. 14.1b). Occasionally, a foreign body giant cell reaction is present (Fig. 14.1c). Besides, a lanugo hair shaft surrounded by inflammatory cells can be identified (Fig. 14.1d). There are intense hyperemia and hemorrhagic foci. The anucleate squamous cells show strong positivity for AE1/AE3 cytokeratin (Fig. 14.1e). Proliferating (reactive) submesothelial spindle cells also display strong positivity for AE1/AE3 cytokeratin. The squamous cells are arranged as single or in groups, and the cheesy exudate is fibrinous.

The predominant type of inflammatory cells depends on the duration of VCP. Neutrophils are predominant soon after delivery. After several days, an acute and foreign body inflammatory reaction will usually be evident. Weeks after delivery, granulomatous foreign body reactions predominate [13, 14].

### 14.3.3 Intraperitoneal Meconium Peritonitis/Granuloma

Differential diagnosis from maternal meconium peritonitis could be difficult due to many similarities. Meconium peritonitis/granuloma characterizes numerous eosinophils scattered irregularly throughout the process. There are many giant cells with organized epithelioid tubercles. Within these cells, vacuoles contain a yellow-brown pigmented material arranged in cords and sheets; the latter stained positive for bile [15].





**Fig. 14.1** (a) Appendiceal biopsy shows normal mucosa, underlying muscularis propria (*black arrow*), and a serosal inflammatory infiltrate (*blue arrows*) centered around fetal squamous cells (*purple arrow*) (H&E;  $\times 20$ ) [16]; (b) Scattered anucleate squamous cells are surrounded by a mixed inflammatory infiltrate. The arrow indicates an anucleate squamous cell (H&E;  $\times 200$ ); (c) Mixed inflammatory infiltrates with the presence of a multinucleated

giant cell. This cell shows rests of squamous cells engulfed in its cytoplasm (H&E;  $\times 200$ ); (d) Lanugo hair shaft amidst inflammatory cells (H&E;  $\times 400$ ); (e) Anucleate squamous cells and proliferating submesothelial cells show strong positivity for AE1/AE3 cytokeratin. The arrow points to an aggregate of anucleate squamous cells (Cytokeratin;  $\times 200$ ) [3]

## 14.4 Pathophysiology

### 14.4.1 Vernix Caseosa Peritonitis/Granuloma

Spillage of VC into the peritoneal cavity incites an inflammatory reaction causing symptoms resembling an acute abdomen. The leakage of amniotic fluid results from the following:

- Antenatal or intrapartum tubal reflux [2, 13],
- Premature rupture of membranes [17],
- Uterine perforation/rupture,
- Rupture of ovarian mature cystic teratoma,
- CS [14].

Tubal reflux of amniotic fluid will not occur unless some disruption of the natural decidual–tubal barrier occurs or intrauterine pressure differences facilitate flow in this direction rather than through the cervix. In the normal gravid uterus of four or more months' gestation, intact membranes, decidual hypertrophy, stromal edema, placentation, and the cervical mucus plug usually occlude the cavity [17].

Most cases were diagnosed in the postpartum period after uneventful CS. The spillage of amniotic fluid into the peritoneal cavity at CS is almost inevitable and usually insignificant. However, in some cases, it can be the trigger for a peritoneal reaction. The exact mechanism leading to the

development of peritonitis is unknown. Meconium (contains anucleate squamous cells and lanugo hair derived from VC) and keratinized squamous cells can induce an inflammatory response. Meconium causes neonatal meconium peritonitis secondary to intestinal perforation [15].

The onset of VCP after uncomplicated CS has been attributed to incomplete peritoneal lavage of spilled amniotic fluid [13]. Keratinized squamous cells can induce an active inflammatory response by mechanical [18] or chemical irritation [19]. A similar presentation is found following the rupture of an ovarian mature cystic teratoma (dermoid cyst), keratinized cysts, and keratinizing neoplasms [20]. The keratin and sebum may provoke an extensive and prominent foreign body reaction that mimics peritoneal carcinomatosis [21], first described by Abitbol et al. in 1959 in a nonpregnant population [22]. Some consider that a higher concentration of VC in amniotic fluid, observed in difficult labors with partial loss of amniotic fluid, or oligohydramnios, may have pathogenic significance [4]. Nevertheless, VC is present in around half (43%) of newborns [23].

On the other hand, a hypersensitivity reaction may occur from sensitization from previous pregnancy and delivery. However, most cases of VCP develop in primiparous women suggesting that a hypersensitivity reaction is less likely [16].

With premature rupture of membranes, the placenta should be examined for acute chorioamnionitis and funisitis [17].

#### 14.4.2 Intraperitoneal Meconium Peritonitis/Granuloma

Intraperitoneal meconium granulomas result from amniotic fluid swallowed during intrauterine life. The ingested fluid is absorbed in the intestine, leaving nondigestible elements such as lanugo and cornified epithelium. This detritus and secretions from the gastrointestinal tract, liver, and pancreas constitute meconium. With

fetal distress and anoxia during a breech delivery, the anal sphincter may relax because of oxygen deprivation, and the fetal intestines will empty. During CS, meconium may spill into the abdominal cavity [24].

### 14.5 Clinical Presentation

Typically, a low parity patient presents 3–35 days following CS [3, 25–28], most after hospital discharge. Pyrexia is common, and nausea and vomiting could be present [29]. The abdominal pain is localized or diffuse [29]. Dyspnea [16] or shoulder tip pain [30] represent diaphragmatic peritoneal irritation. Patient after vaginal delivery presented 3 hours post-delivery [2]. Physical examination reveals diffuse or lower quadrant abdominal tenderness and often positive Blumberg's sign [3]. The vaginal examination does not reveal pathology (almost all patients delivered by CS). The severity of clinical presentation depends on the quantity and dissemination of VC material [3, 25, 26, 30].

Probably some patients go unrecognized with the subclinical presentation. Some patients report discomfort, mild abdominal pain, or low-grade fever as the only symptom. These symptoms are present in numerous, more common postpartum processes, and subclinical or mild VCP is not even suspected [14].

The third type of presentation is a chronic form with sinuses or granulomas, mainly in a CS scar (Fig. 14.6a) or even after exploration and extensive peritoneal lavage of all focuses of VC (see Sect. 14.9.1).

### 14.6 Differential Diagnosis

The differential diagnosis depends on clinical examination results or diagnostic imaging methods used. Clinical examination results in two groups of differential diagnoses, whether the presentation involves peritonitis or peritoneal granulomas. Peritonitis mainly presents with maximal pain and tenderness in the young female population in the lower right quadrant [17, 31].

**Table 14.1** Differential diagnoses of vernix caseosa peritonitis [3, 15, 16, 28, 32, 33]

| Peritonitis                        | Granuloma                              |
|------------------------------------|----------------------------------------|
| Acute appendicitis                 | Scar endometrioma                      |
| Acute cholecystitis                | Suture granuloma                       |
| Ruptured ovarian cyst              | Starch glove granuloma                 |
| Hollow organ perforation           | Abdominal tuberculosis                 |
| Bowel injury                       | Carcinomatosis                         |
| Endometritis                       | Disseminated peritoneal leiomyomatosis |
| Pelvic inflammatory disease        |                                        |
| Starch glove peritonitis           |                                        |
| Meconium granulomatous peritonitis |                                        |

Therefore, acute appendicitis is the most common preoperative diagnosis (Table 14.1). Postpartum fever, with or without peritoneal signs, is usually attributed to “endometritis.” Without apparent clinical signs, VCP may go unrecognized and undocumented. Peritoneal deposits on imaging mimic peritoneal carcinomatosis or tuberculosis. Disseminated peritoneal leiomyomatosis probably develops after laparoscopic myomectomy, in addition to the role of estrogen. Fragments from the morcellation of myoma left in the peritoneum would be capable of inducing metaplasia of the peritoneal mesenchymal cells, and particularly vulnerable women could develop it.

**14.7 Diagnosis**

Clinical presentation with additional diagnostic workup may raise a suspicion of VCP and potentially prevent unnecessary removal of healthy organs at laparotomy.

Cultures are negative, and antibiotics do not affect the fever or white blood cell count [5].

**14.7.1 Laboratory Findings**

Leukocytosis and neutrophilia are always present [3]. Vaginal, urinary, hematological, serum, and tissue microbiological specimens are negative [1, 16, 25, 34]. There are cases with elevated CA-125 [30].

**14.7.2 Diagnostic Imaging**

Diagnostic imaging methods commonly show nonspecific changes or normal findings, especially during the first few days of the disease.

**14.7.2.1 Plain X-Rays**

A plain abdominal X-ray is not diagnostic and primarily defines the consequences of peritonitis or partial bowel obstruction—air–liquid levels [1, 27]. Due to pleuritic pain, dyspnea, or shoulder tip pain, patients undergo chest X-rays or thoracic CT, which is always normal [30].

**14.7.2.2 Transabdominal Ultrasound**

This is the first diagnostic modality of choice, but it is nonspecific. In some cases, free fluid is present in an amount larger than normal. In rare cases, larger deposits can be revealed (Fig. 14.2), but



**Fig. 14.2** An echogenic oval lesion indenting the hepatic capsule lies between the liver parenchyma and abdominal wall. (Reproduced with permission from [30])



without the possibility of accurate diagnosis. Some gastrointestinal causes can be ruled out, such as acute cholecystitis.

#### 14.7.2.3 Abdominal CT

The CT appearance of VCP has not been well-defined or well-reported. Also, <50% of patients underwent abdominal CT [5]. Abdominal CT of proven VCP shows normal findings in 16%, while most remaining cases described nonspecific findings [5]. Possibly, the CTs were performed too early to demonstrate peritoneal nodules [5].

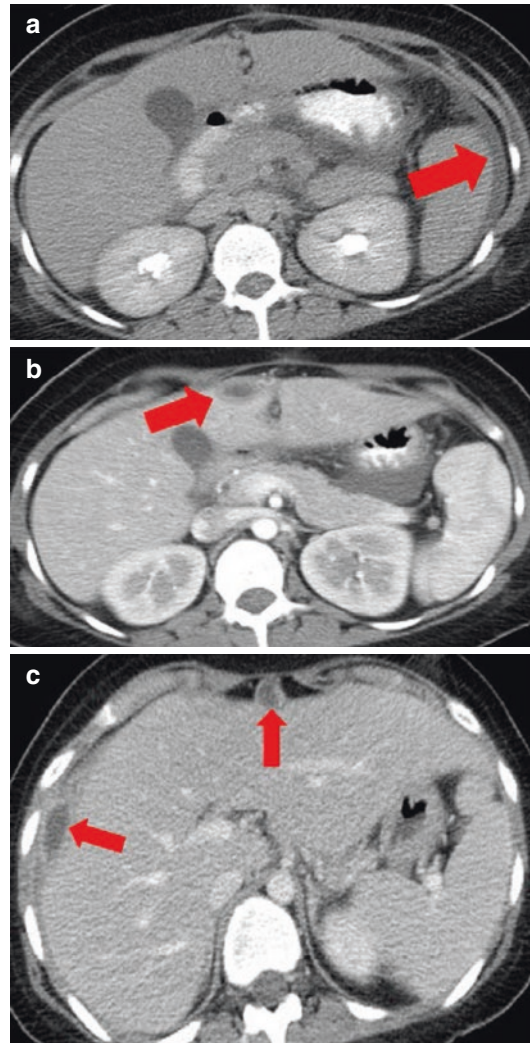
Contrast-enhanced abdominal CT reveals multiple oval rim-enhancing peritoneal lesions misinterpreted as peripheral hepatic metastases, peritoneal carcinomatosis (which can be excluded with a high level of certainty due to normal intra-peritoneal status during recent CS), or abdominal tuberculosis [35]. Abdominal CT made during the first several days commonly shows a small amount of free fluid (Fig. 14.3a) because neutrophils are predominant soon after delivery. After several days, an acute and foreign body inflammatory reaction starts, forming multiple oval rim-enhancing peritoneal lesions (Fig. 14.3b). These lesions progress in number and size [5, 30]. Subsequent abdominal CT made for persistent symptoms shows an increase in the number and size of such lesions (Fig. 14.3c).

#### 14.7.2.4 Abdominal PET-CT

In complicated medical, gynecological, or surgical history, even PET-CT is made with high glucose uptake suggesting malignancy (Fig. 14.4) primarily due to the mass irregularity. High glucose uptake is due to the inflammatory origin of VCP (flow cytometry demonstrated that M1-polarized glut+ macrophages were the most dominant cell subsets) [36].

#### 14.7.2.5 Abdominal MRI

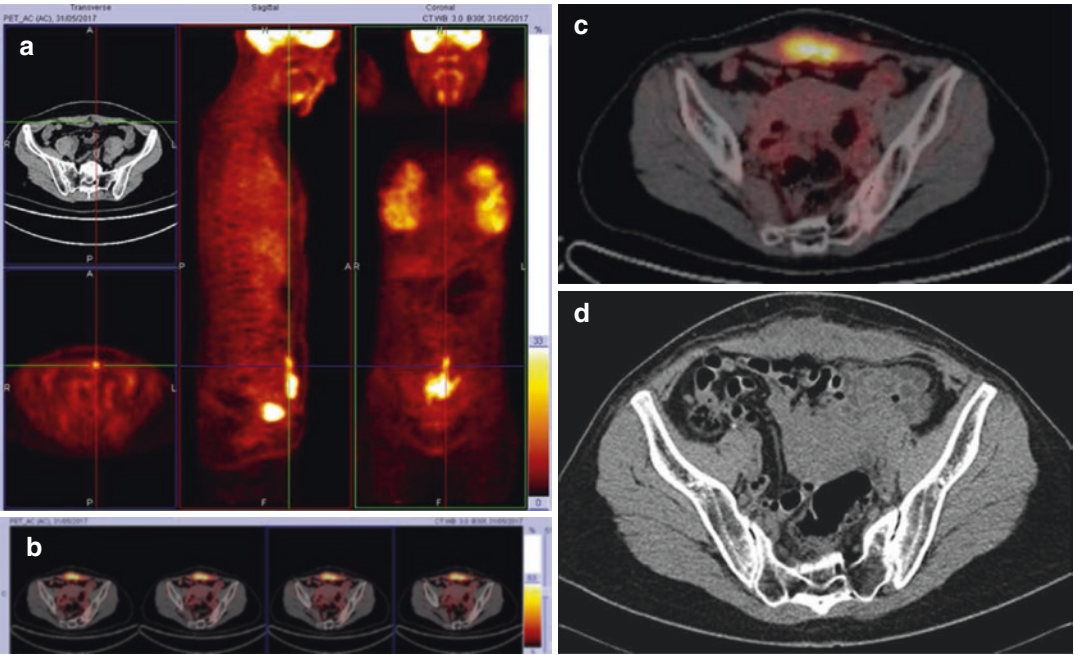
MRI can define peritoneal nodules (Fig. 14.5), but there are no VC pathognomonic MR findings. Except for diagnosis, MR serves as a follow-up after conservative therapy, estimating the decrease in peritoneal nodule size (Fig. 14.6).



**Fig. 14.3** (a) Abdominal CT on postoperative day 4 shows only a small amount of ascites (arrow). (b) Abdominal CT on postoperative day 9 at the same level shows a new small, well-defined, peripherally enhancing cystic nodule anterior to the liver (arrow). (c) Abdominal CT on postoperative day 14 shows two new small, well-defined, peripherally enhancing cystic perihepatic nodules (arrows). (Reproduced with permission from [5])

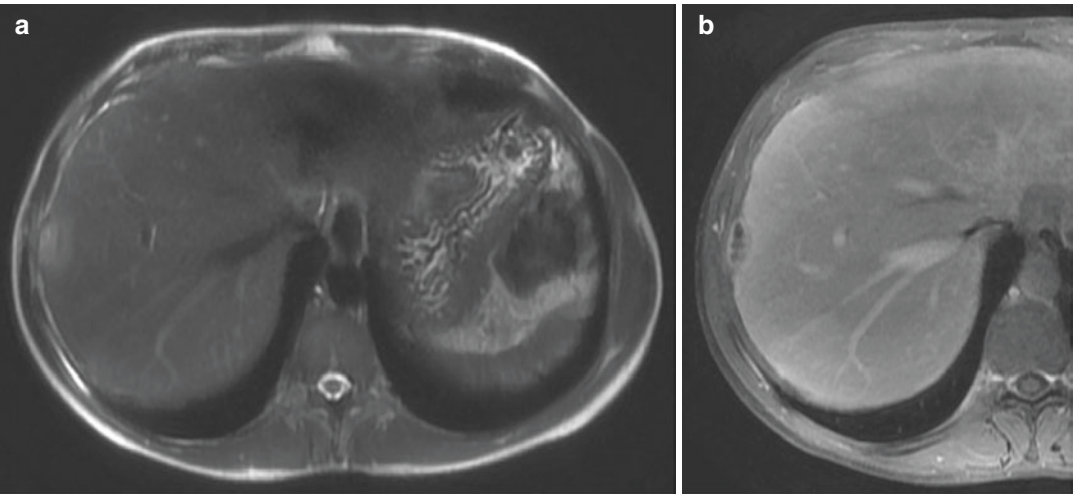
#### 14.7.3 Fine-Needle Aspiration

In the chronic course, fine-needle aspiration reveals a mixed inflammatory response and a few anucleate and mature squamous cells, granulation-type tissue. This confirms the diagnosis of VCP or VC granuloma [30].



**Fig. 14.4** Preoperative PET (a–c) and CT (d) show the irregular mass in the lower part of the rectus muscles of the abdomen. The PET shows an area of irregular and inhomogeneous hypercaptation in the context of the for-

mation of the anterior abdominal wall with a very high maximum standardized uptake value (SUV max up to 12.9). (Reproduced with permission from [36] under the CC Attribution License)



**Fig. 14.5** (a) T2-weighted MRI shows a juxta-hepatic lesion with an increased T2 signal. (b) Post-gadolinium fat-saturated T1-weighted MRI shows peripheral contrast

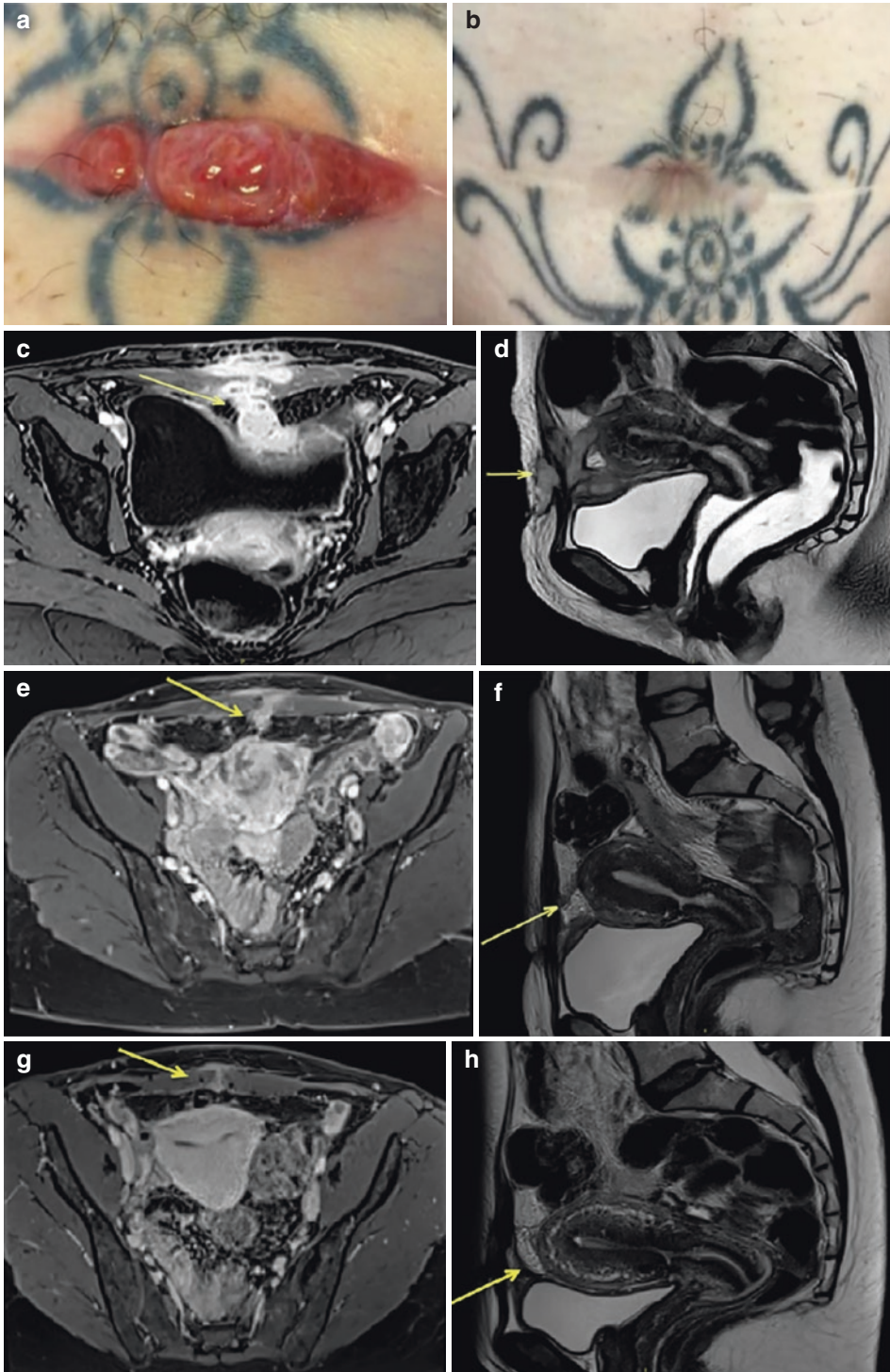
enhancement of the juxta-hepatic lesion with central low T1 signal. (Reproduced with permission from [30])

### 14.7.4 Diagnostic Exploration

Diagnostic laparoscopy or laparotomy to exclude common conditions (acute appendicitis, ruptured viscus, bowel, or ureter injury) shows character-

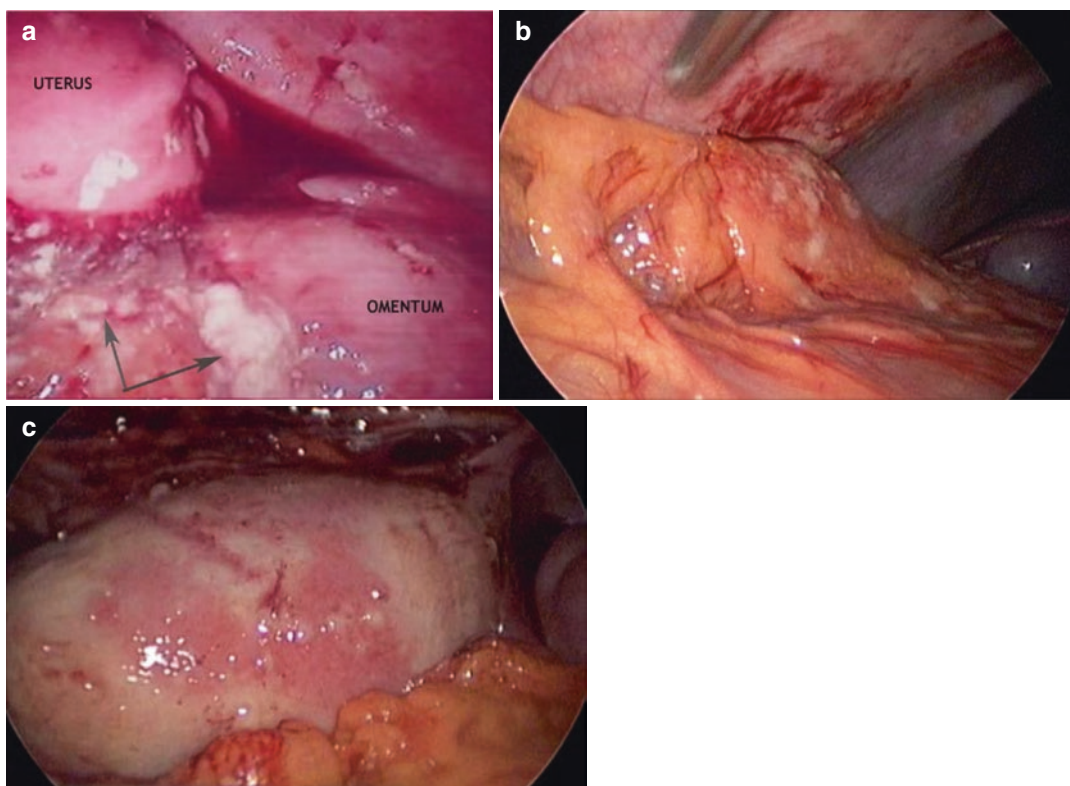
istic white and yellow cheese-like plaques (Fig. 14.7) deposited on visceral and parietal peritoneal surfaces throughout the abdominal cavity, in the absence of inflammation or perforation of viscera. A non-purulent peritoneal collec-





**Fig. 14.6** Scar (a) 3 months and (b) 20 months after the CS. (c) Pelvic MRI 3 months after the CS, axial T1-weighted sequence contrast-enhanced with fat suppression. (d) Pelvic MRI 3 months after the CS, sagittal T2-weighted sequence. (e) Pelvic MRI 6 months after the CS, axial T1-weighted sequence contrast-enhanced with

fat suppression. (f) Pelvic MRI 6 months after the CS, sagittal T2-weighted sequence. (g) Pelvic MRI 13 months after the CS, axial T1-weighted sequence contrast-enhanced with fat suppression. (h) Pelvic MRI 13 months after the CS, sagittal T2-weighted sequence [4]



**Fig. 14.7** (a) Vernix caseosa deposits scattered throughout the peritoneal cavity (gray arrows) in a diagnostic laparoscopy. (Reproduced with permission from [16] under the CC BY 2.0). (b) Vernix caseosa plaques were found scattered on the surface of the omentum. These

plaques were associated with loose adhesions to the anterior abdominal wall. (c) Cheesy white exudate covering the surface of the uterus. There is no inflammation of the underlying tissue. (Reproduced with permission from [37])

tion may be present. The cheesy exudate was present in all patients [29]. Peritoneal or omental biopsies and biopsies of white serosal patches are diagnostic (see Sect. 14.3).

Another advantage of diagnostic laparoscopic is the possibility of converting to Pfannenstiel or midline incision, depending on the underlying pathology. Many nonobstetrical and obstetrical conditions, such as a ruptured uterus, cannot be repaired by laparoscopy.

## 14.8 Treatment

### 14.8.1 Conservative Treatment

The nonoperative management is rarely initiated because pretreatment diagnosis is challenging and commonly attributed to other causes of acute abdomen. Some patients were treated nonoperatively

with analgesia and antibiotics, but exploration was performed due to the worsening of symptoms [16]. Possible contraindications could be the complications that arise from residual VC even after exploration and its removal (see Sect. 14.9.1).

Some recommend postoperative antibiotic therapy [17, 18, 26, 28, 38]. However, uneventful cases without perioperative antibiotics [3] are probably due to (1) the chemical nature of the peritonitis and (2) at least 10 peptides within VC with antibacterial properties [39, 40]. Abdominal swabs are always negative (see Sect. 14.7.1). Even the administration of adjuvant steroid therapy for resistant symptoms without infection has been proposed [38]. The notable response is observed with steroid use for 1–2 weeks, gradually tapering off over the next 2 weeks [38]. It is postulated that steroids significantly enhance the clinical course by suppressing the inflammatory response. This concept is successful even in conservatively



treated patients after unsuccessful antipyretic and antibiotic therapy with objective improvement on abdominal MR [4]. Similar therapy confirms maternal intraperitoneal meconium peritonitis/granulomas with the addition of nonsteroid anti-inflammatory drugs [15]. However, these various treatments remain empirical and controversial.

## 14.8.2 Surgical Treatment

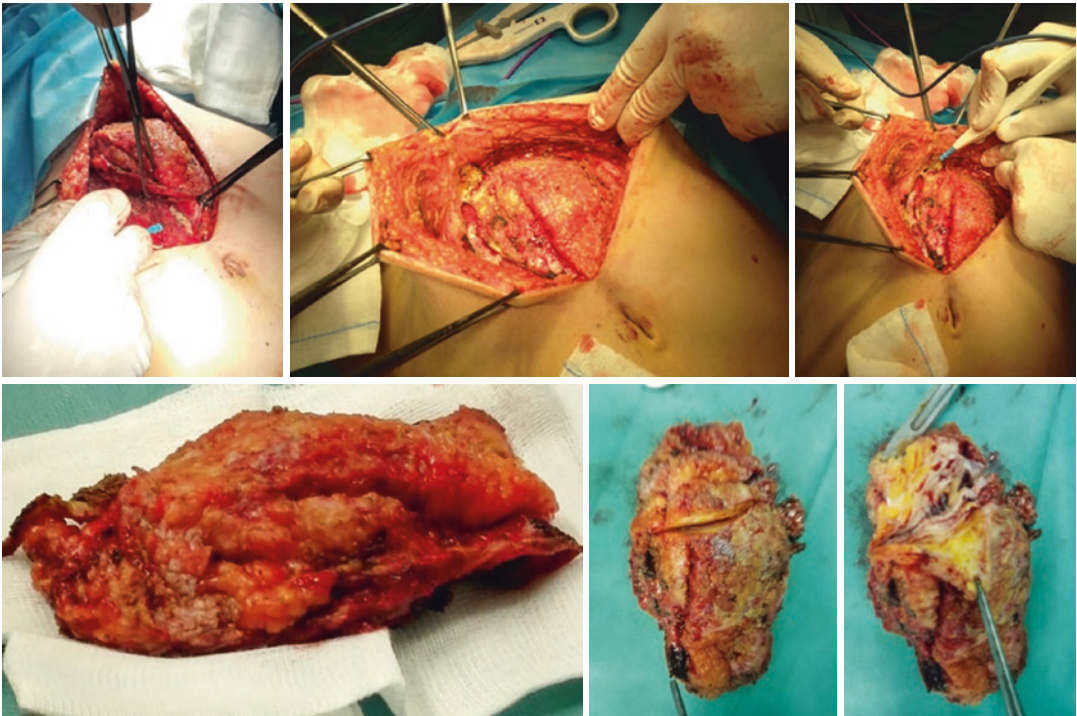
### 14.8.2.1 Vernix Caseosa Peritonitis

Laparotomy is performed in 88% when numerous areas of cheese-like fibrinous exudates are seen on the serosal surface of the viscera [4]. Commonly appendix is covered with exudate, and acute appendicitis is a typical intraoperative diagnosis. Therefore, appendectomy and extensive peritoneal lavage are routinely performed even when VCP is recognized [27]. Awareness of

the characteristics of VCP helps to avoid extensive excisional procedures (64%) [4] with suspicion of other processes, such as total hysterectomy, salpingo-oophorectomy, cholecystectomy, or partial colectomy, with subsequent normality in the histopathological study of these organs [14, 28, 34]. Therefore, pathologists are essential for correct diagnosis with intraoperative or deferred consultation. Unnecessary, additional procedures add to perioperative morbidity and compromise recovery [16].

### 14.8.2.2 Vernix Caseosa Granuloma

With chronic presentation, the granulomatous changes can occur as sinus tracts or palpable abdominal wall masses (Figs. 14.4 and 14.8 Lower row). With the potential of malignancy, radical excision is common with challenging adequate abdominal wall closure (Fig. 14.8 Upper row).



**Fig. 14.8** (Upper row) Intraoperative pictures of abdominal wall vernix caseosa granuloma. The mass started from the anterior sheath of the rectus muscle of the abdomen and extended to the fatty tissue of the subcutaneous

layer. (Lower row) Macroscopic view of the excised abdominal wall mass weighing approximately 300 g and sized  $11 \times 10 \times 4$  cm. (Reproduced with permission from [36] under the CC Attribution License)

## 14.9 Prognosis

### 14.9.1 Maternal Outcome

Even after exploration and irrigation/suction of the entire intraperitoneal cavity, consequences of intraperitoneal VCP could develop. These primarily present in the form of small bowel obstruction, sometimes with recurrent episodes [16], wound discharge [16], or chronic VC sinus [16].

The sequel is common with operative and nonoperative treatment. The sinus tract of proven VC should be excised, together with abdominal mass, if found on preoperative imaging [16]. The operative intervention should eliminate recurrent or intermittent abdominal pain due to adhesions [16]. The location of VC granuloma determines the type of operation. Abdominal wall granuloma [36] should be excised, while intraperitoneal granuloma sometimes requires bowel resection [41]. In such cases, fine-needle aspiration reveals a mixed inflammatory response, scattered foci of anucleate keratin/squames confirmed by a cytokeratin immunostain, a few anucleate and mature squamous cells, and a granulation-type tissue [30]. Also, PET-CT can define lesions without a definitive preoperative diagnosis [36].

### 14.9.2 Fetal Outcome

Almost all cases develop and present several after CS. Therefore, the delivery and the fetus are not compromised by the VCP.

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## Part III

## Surgery

## Abstract

Acute appendicitis is the most common non-obstetric operative emergency during pregnancy. It amounts to 25% of operative indications for the acute abdomen during pregnancy and puerperium. Pain in the right lower quadrant is the most reliable symptom, and abdominal tenderness is almost always present. Fever and tachycardia are not sensitive signs. Leukocytosis is not diagnostic because elevated levels are found during pregnancy, especially in the early labor in normal pregnancy. Neutrophil granulocytosis is diagnostic as it is a sign of bacterial infection. Graded abdominal ultrasound is the diagnostic procedure of choice with less accuracy in the third trimester with no guidelines about the use of transvaginal ultrasound. Magnetic resonance imaging is the diagnostic procedure of choice in cases when an abdominal ultrasound is not diagnostic. Nonoperative antibiotic treatment is increasingly used with excellent outcomes during pregnancy. A laparoscopic approach is increasingly used without adverse fetal outcomes. Fetal mortality in uncomplicated appendicitis is low and raises several times when perforation and diffuse peritonitis develops. Maternal mortality is almost 0% and increases with the delay in surgery for more than 24 h, which is the most common

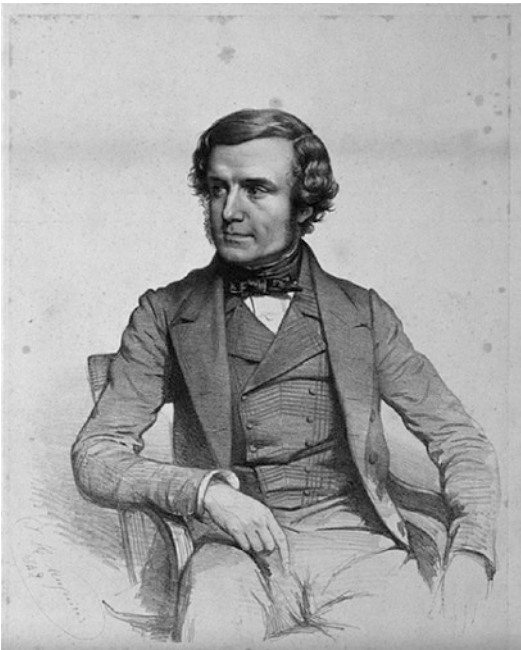
situation in the third trimester when the diagnosis is often delayed and inaccurate.

## 15.1 Historical Perspective

*It proves fatal to a woman in a state of pregnancy if she is seized with any acute diseases.*

(Hippocrates)

In 1836 (reference unavailable), Stumpf described a rupture of the cecum in a pregnant woman, which could be a perforated acute appendicitis (AA). Officially, the first case was in 1848, when Henry Hancock (Fig. 15.1), the President of the Medical Society of London, presented a paper to that society describing the treatment of a 30-year-old woman, in her fifth pregnancy, 7 months pregnant bearing twins in the Charing Cross Hospital in London [2]. She developed abdominal pain, had preterm labor on the fourth day with a live newborn for 20 h, and developed a tender mass in the lower right abdomen. She was seen by Hancock 12 days after the disease had started. She had a distended, tender abdomen, particularly in the lower right quadrant (RLQ). Hancock prescribed opium and poultices. Two days later, her condition was much worse, with a palpable mass in the RLQ. The incision was made above and parallel to Poupart's ligament over the palpable mass. During exploration, offensive pus and bubbles of gas escaped. After 2 weeks, she felt pain around the wound, and



**Fig. 15.1** Henry Hancock (1809–1880). Lithograph by T. H. Maguire, 1849. (Reproduced with permission from [1] under the CC BY 2.0)

after wound exploration, Hancock found two fecaliths. He postulated that fecaliths had escaped by ulceration from the diseased appendix. From that time, her improvement was rapid, and she made a good recovery.

Wiggin, in 1892, reported the first case of preoperative diagnosis and an operation advised at a time when the life of both mother and infant could have been saved. Unfortunately, the patient’s friends refused the operation. Petersen, in 1893, recorded the first postpartum case of AA on the seventh day following labor at term, with rupture of the abscess into the bowel and recovery without operation [3]. In 1894, Paul Fortunatus Mundé (1846–1902), a gynecologist from Mount Sinai Hospital in New York, published the first successful case from the USA [4], treating appendiceal abscess but with the premature delivery of a dead child. Spirtos et al. published the earliest series of laparoscopic appendectomies (LA) during pregnancy in 1987 [5].

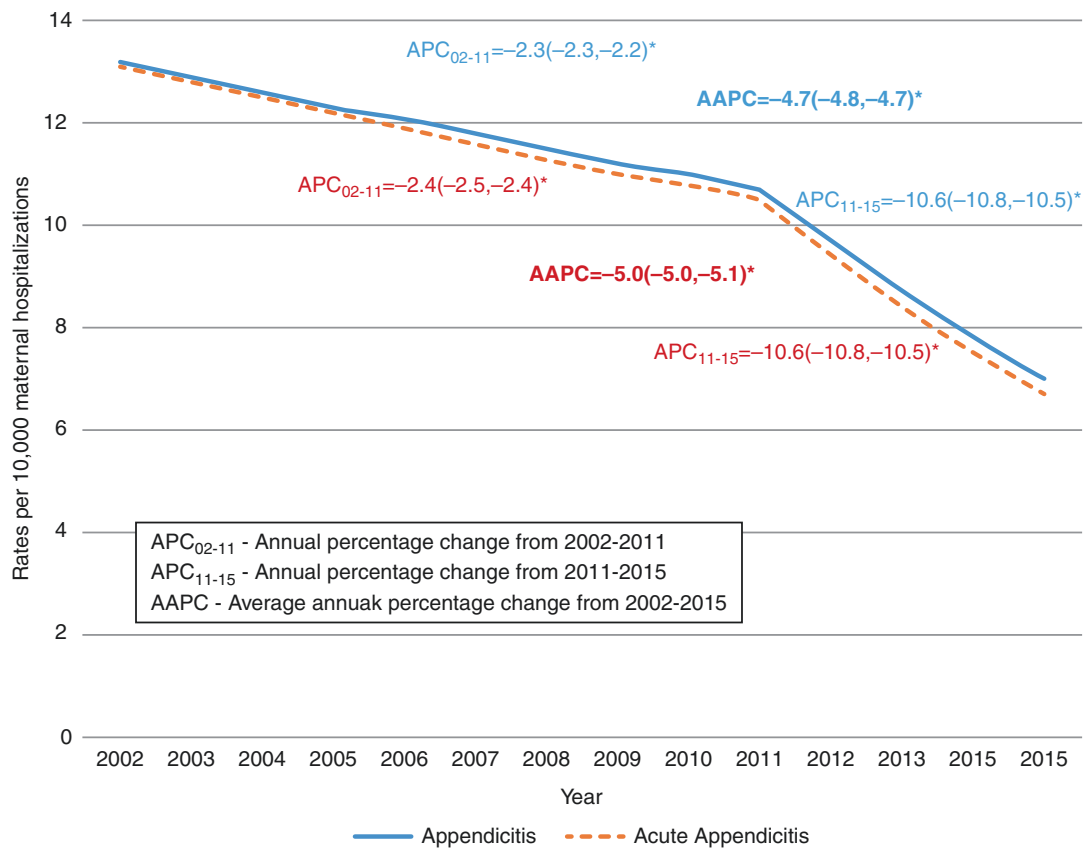
15.2 Incidence

*Appendicitis seems to be favored by pregnancy /  
L’appendicite semble favorisee par la grossesse.*  
(Dieulafoy)

Appendicitis or epityphlitis (*epi* - + Greek *typhlon* = cecum + - itis, inflammation) is the most common non-obstetric cause of acute abdomen during pregnancy and puerperium. Between 1913 and 1926, approximately 2–2.5% of the women who presented with symptoms of AA were pregnant [6, 7]. Since 1935, the incidence of AA during pregnancy was 1/2000 [8], while between 1944 and 1959, the incidence was 1/1000 [9, 10]. The report from 1972 claimed 1/704 [11]. The conclusion was that AA is a disease of modern civilization caused by a sedentary life and a high-residue flesh diet [12]. Current incidence estimates range from 1/181 to 1/8770 pregnancies. AA amounts to 25–30% of operative indications for the acute abdomen in pregnancy [13–32]. The rate of AA during pregnancy in the most recent four population-based studies is 1/1000–1/4167 pregnancies [22, 27, 33, 34]. The highest incidence is in Taiwan—1/181 [13] and varies significantly between countries and even between regions and hospitals in the same country (Table 15.1). Although no references specifically address postpartum AA, most studies group AA in pregnancy and the puerperium because of the anatomic and physiological continuum [38]. In the USA (2002–2015), there

**Table 15.1** Comparative incidence of acute appendicitis in pregnancy between countries

| Country           | Incidence    |
|-------------------|--------------|
| Taiwan [13]       | 1:181        |
| Pakistan [25, 35] | 1:346–1:1135 |
| Germany [24]      | 1:499        |
| Sweden [29]       | 1:776        |
| Chile [36]        | 1:1028       |
| Israel [37]       | 1:1055       |
| Saudi Arabia [28] | 1:1102       |
| Turkey [15]       | 1:1312       |
| Jordan [31]       | 1:1644       |
| Brazil [32]       | 1:2580       |
| Mexico [30]       | 1:8770       |



**Fig. 15.2** USA trends in rates of all appendicitis and acute appendicitis per 10,000 maternal hospitalizations (2002–2015). (Reproduced with permission from [39])

was a 5% average annual decrease in AA rates, with a steep decline in overall appendicitis and AA rates after 2011 (Fig. 15.2). The trimester analysis is presented in Sect. 15.3.2.

### 15.3 Risk Factors

#### 15.3.1 Age and Multiple Pregnancies

A higher incidence of AA in pregnancy than other causes is multifactorial (Table 15.2). The incidence of AA and childbearing are strongly related to a younger age. Ninety percent of pregnant women are <30 years [40], correlating with the peak incidence of AA in the general population [41]. The incidence of AA shows regional variations and a secular trend with a decreasing incidence in the general population. Secular and

**Table 15.2** Risk factors for acute appendicitis during pregnancy

|                                            |
|--------------------------------------------|
| Age <30 years                              |
| Multiple pregnancies                       |
| Second trimester (perforated and negative) |
| Black and Hispanic women                   |
| Nonobese                                   |
| Attacks of appendicitis before pregnancy   |
| (pregnancy-induced) constipation           |
| Medicaid insurance                         |

regional variations are related to the incidence of childbirth. The influence of these variations on the incidences of AA and pregnancy is complex, making it difficult to determine the expected incidence of AA during pregnancy for comparison purposes. Early marriage and repeated pregnancies till menopause increase the probability of an AA in pregnancy.

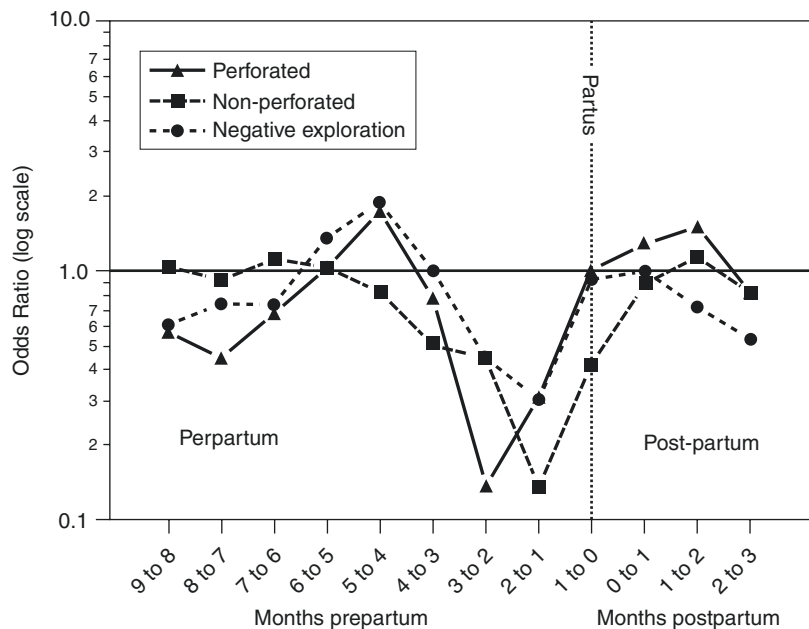
### 15.3.2 Trimester

It seems that AA is more common in the second trimester with an incidence of 35–50% [24–26, 42, 43] (the first 30%, the second 45%, and the third 25% [22, 40, 44, 45]), but there is no proof that pregnancy affects the overall incidence [46]. Figure 15.3 compares appendectomies across trimesters of pregnancy to matched controls [47]. Patients who had undergone appendectomy were less likely to be pregnant at the operation than controls. This inverse relation depended on the gestation period and the underlying diagnosis at the operation. Corroborating results from previous reports, the highest incidence of AA and appendectomy was found in the second trimester of pregnancy. This pattern was seen for perforated AA and negative explorations, whereas for non-perforated AA, the strength of the inverse relation increased continuously throughout the pregnancy. This result suggests that pregnancy may protect against AA (Fig. 15.3). In the largest study to date, a national representative cohort of almost 1.6 million child-bearing women, pregnant women during the antepartum period were 35% less likely to be

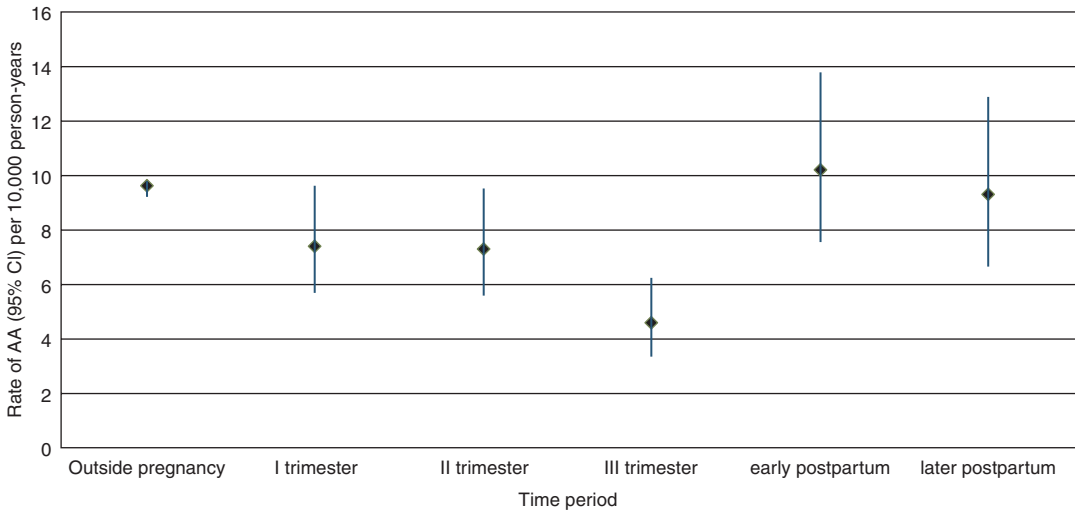
diagnosed with AA than the time outside pregnancy (Fig. 15.4), with the lowest risk reported during the third trimester.

Results were unchanged after adjusting for age and calendar year. Furthermore, there is no increased risk of AA in the puerperium than outside pregnancy among women aged 15–34. However, the risk increased almost twofold in older women during the latter postpartum [33]. It is possible that AA during pregnancy, at term, and in the puerperium is lower or underestimated. First, it could be an unrecognized mild, self-limiting disease [48–50]. Mild attacks could be interpreted as the ordinary discomforts of pregnancy, and the severe cases in the puerperium were probably regarded as types of puerperal sepsis. Also, these attacks could be interpreted as intestinal colic, renal colic, ureteropyelitis, threatened miscarriage, salpingitis, and tubal pregnancy. The second is the issue of AA during term labor. Sometimes, labor is induced by inflammatory changes due to AA (see Chap. 4) [49]. The third is potentially reduced incidence, especially in the third trimester, because of the protective (immunomodulatory) effect of pregnancy (see Sect. 15.4.1) [47]. This fact dates back

**Fig. 15.3** Comparison of gestational age in women who had an appendectomy compared with matched controls. The relation is expressed as the odds ratios according to conditional logistic regression. (Reproduced with permission from [47])







**Fig. 15.4** Absolute rates of acute appendicitis per 10,000 person-years by trimesters and the early and later postpartum period in England. (Reproduced with permission from [33])

to 1921 with the conclusion that *in the last few weeks of gestation and during labor, it is very rare* [51]. It was found at term in 1% [52].

### 15.3.3 Other

A significantly higher proportion of Black and Hispanic women have AA during pregnancy [34]. In 1905, conservatively treated suspected acute or chronic appendicitis had a significantly higher incidence of AA during pregnancy, up to 50% (see Sect. 15.4) [48, 53, 54]. Pregnant women with AA were less likely to be obese and more commonly had Medicaid insurance [34]. Constipation is a risk factor in the nonpregnant and pregnant population [55]. Constipation, a major risk factor, was recognized in 1897 when R. Abramhams collected 15 cases [56].

## 15.4 Pathogenesis

One mechanism of AA is the mechanical obstruction of the appendiceal lumen, either due to fecal stasis, kinking peritoneal adhesions, or infection-induced swelling of the mural lymphoid tissue. Another mechanism is a breakdown of the appendiceal mucosal barrier by the direct invasion of a

pathogen or by an inflammatory response triggered by an infectious agent or some other stimulus. Geographical differences in the incidence of AA and secular trends in the general population have been related to the differences in fiber dietary intake and hygiene standards [57, 58].

### 15.4.1 Immunologic Changes

During pregnancy, a range of physiological changes may influence the pathogenesis of AA. The implantation requires a T-helper cell type 1 (Th<sub>1</sub>) response, followed by a shift toward a Th<sub>2</sub> phenotype for the main duration of pregnancy and a Th<sub>1</sub> milieu toward partition [59]. This shift toward a Th2-dominated immunity results in a depressed cellular inflammatory response and increased humoral immunity [60]. There is an overall decrease in proinflammatory cytokine trajectories in the innate and adaptive arms of the immune system and an increase in counter-regulatory cytokines as the pregnancy progresses [61]. Because AA is an inflammatory process, the inverse relationship between pregnancy and AA could suggest that a Th1-mediated inflammatory response is partly responsible [62]. This mechanism influences only the inflammatory and not obstructive type of AA.

Moreover, cigarette smoking has a proinflammatory effect [63] and is associated with an increased AA risk in the general population [64]. Because pregnancy may motivate women to quit smoking [65, 66], this could also partially contribute to the lower risk of AA observed during pregnancy. Inflammatory markers have a dose-dependent and temporal relationship to smoking and smoking cessation. The smoking-associated inflammatory response returns to normal 5 years after smokers quit [67].

### 15.4.2 Anatomical/Physiological Changes

In the general population, the incidence of AA is higher in men. It has been suggested that the vascular anastomoses in women between the blood vessels of the appendix and the ovarian vessels on the right side may induce comparative immunity. These anastomosing channels relieve appendiceal congestion and inflammation by carrying some blood into systemic circulation [53]. This mechanism does not have any effect on the obstructive form of AA.

Progression of AA may be more fulminating in pregnancy. Increased pelvic vascularity and displacement or kinking (especially if partly fixed) of the appendix by the growing uterus may hasten obstruction or strangulation. An increased local lymphatic drainage and interference with omental migration due to the enlarged uterus may favor the systemic spread of the inflammatory process. *Braxton Hicks contractions* prevent the formation of adhesions, thereby promoting early diffuse peritonitis [20, 40, 68, 69]. Also, suppuration takes place higher in the abdomen. The abdomen can handle suppuration much better in the lower than in the upper parts. When inflammation and suppuration occur, abdominal viscera localize the process by encircling it. In pregnancy, the intestines and greater omentum are dislocated. Also, the abdominal viscera strive to localize the process, decreasing its movements. At the same time, the uterus does the reverse

increasing the possibility of spreading suppuration and making diffuse peritonitis more likely. The adnexa and appendix are brought closer with the ascent of the uterus. Infection in either may cause a corresponding inflammation in the other by contiguity. In 1900, the communication by lymphatics, by a *peritoneal fold of Clado*, the appendicular ovarian ligament was claimed. This is a fold of the peritoneum, prolonged outward from the infundibulopelvic ligament to the meso-appendix [70].

Another possibility for the spread of localized infection is immediately after delivery. The expulsion of the fetus and sudden contraction of the uterus promote abscess rupture. König and Muret made early observations of this phenomenon [71].

### 15.4.3 Recurrent/Chronic Appendicitis

Pregnancy does not predispose to the first attack of AA [48, 53–55] but increases the risk of recurrent AA during the same pregnancy. Théodore Tuffier, in 1897, reported a woman with three successive pregnancies accompanied by appendiceal attacks [72]. The resection of the appendix, which contained a concretion, was curative. Recurrent attacks in pregnancy could be the result of vascular engorgement of the appendix, constipation commonly associated with pregnancy, the toxemias of pregnancy, the encroachment of the uterus in the early months of pregnancy and puerperium, and the occasional stretching or breaking down old inflammatory adhesions, binding the appendix to the uterus and its appendages. Although without proper analysis, Melford B. Jorgensen in 1952 stated that (1) recurrent AA is relatively frequent in pregnancy, and as the pregnancy advances, the attacks become increasingly more severe, with more difficulty in diagnosis and the surgical procedure more difficult; and (2) AA is likely to recur in pregnancy if there has been a previous attack [73]. The history of AA was present in up to 15%

[42]. Recurrence of AA occurs even after antibiotic treatment during (2.9%) the same pregnancy [42, 74, 75] or after (5.9%) delivery [42], with an overall recurrence of 8.8% [42].

#### 15.4.4 Female Sex Hormones

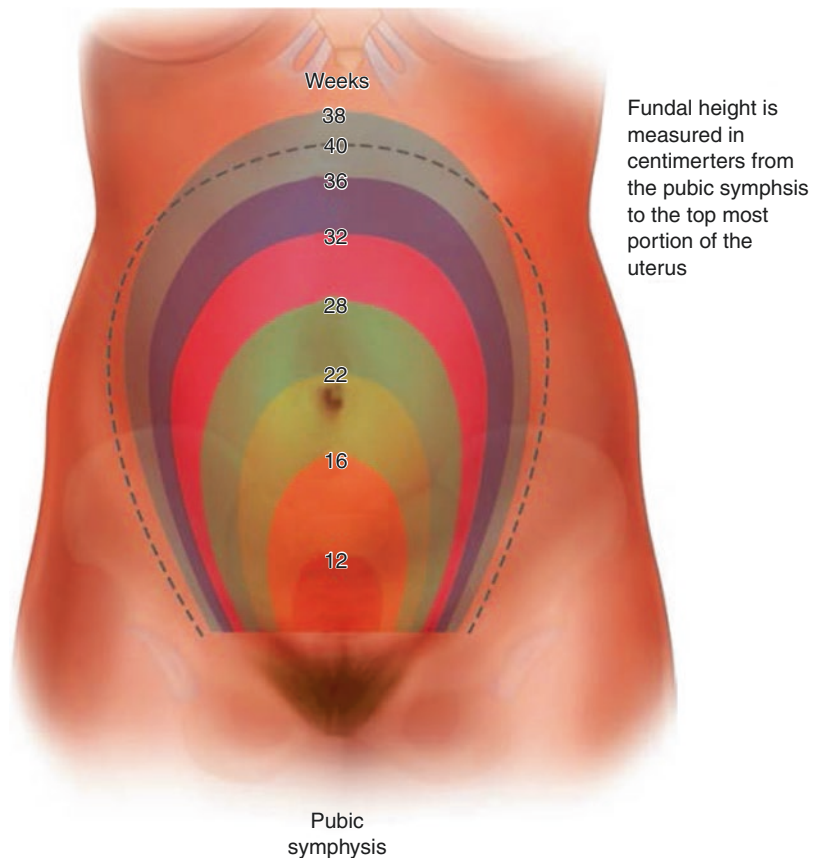
A relation with female sex hormones has been proposed because of a lower incidence among women and incidence variations during the menstrual cycle, but with inconsistent results [76, 77]. This observation was presented first by Le Genre in 1897. Childbearing constitutes a period of many hormonal fluctuations. The dynamic maternal immune responses to normal pregnancy have evolved out of the need to support a semi-allogenic fetus throughout the pregnancy without significant infectious or inflammatory impediment to the mother.

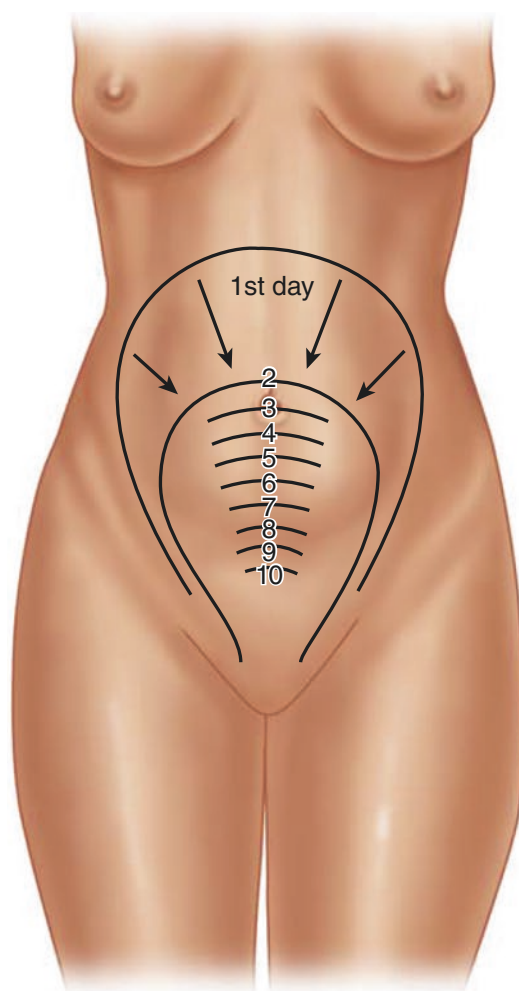
## 15.5 Clinical Presentation

### 15.5.1 Medical History

The approach to pregnant patients with abdominal pain is similar to nonpregnant patients. However, the anatomical/physiological pregnancy-related changes must be considered when interpreting history and physical examination findings. The uterus enlarges about 20 times during pregnancy resulting in stretching of supporting ligaments and muscles and pressure on other intra-abdominal structures and layers of the anterior abdominal wall (Fig. 15.5). Immediately after delivery, the uterus assumes a 15–16-week size [79]. At 1 week postpartum, the uterine fundus returns to the pelvis and is the size of a 12-week gravid uterus. After the first week, uterine involution occurs more slowly, reaching pre-pregnancy size within 6 weeks (Fig. 15.6).

**Fig. 15.5** Height of the fundus at comparable gestational dates varies greatly. The most common heights are shown. A convenient *rule of thumb* is that at 5 months gestation, the fundus is usually at or slightly above the umbilicus [78]





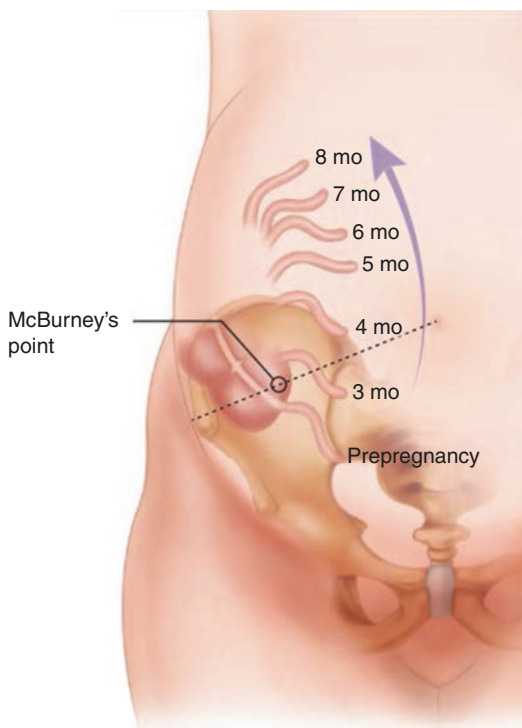
**Fig. 15.6** Postnatal shrinking of the uterus

During the first 6 months of pregnancy, symptoms and signs of AA are the same as in nonpregnant women, but diagnostic difficulties remain due to the following:

- Blunting/masking of symptoms and signs (abdominal distension, intra-abdominal organ dislocation, diminished tissue response to inflammation),
- Possible changes in appendiceal location as pregnancy advances,
- Nausea, vomiting, and abdominal pain of normal pregnancy, especially in the first trimester,

- Extensive differential diagnosis with the addition of pregnancy-related diseases,
- Working diagnosis of systemic infection,
- Obstetric complications could be the first sign of non-obstetric intraperitoneal infection.

*Constant abdominal pain* is the most common symptom [17], and RLQ pain, present in 67–84%, is the most reliable symptom [17, 20, 21, 29, 40, 80]. The incidence of RLQ pain decreases during trimesters (100%, 80%, and 60%, respectively) [81]. Rates of pain localized in the RUQ range from 10 to 42% [40, 82, 83] and are most common during the third trimester [25]. Classical pain migration is found in 50–70% [29, 84]. After the third month of pregnancy, the pain could change location and migrate progressively upward and laterally, reaching the level of the right iliac crest at the end of the sixth month of pregnancy. Füh, in 1905 and 1913, described the displacement of the cecum and appendix upward [82, 83]. At that time, Hoffman, in 1920, stated that the appendix is below the iliac crest in 90% of pregnant women and that the exact position of the cecum during pregnancy can be defined only by abdominal X-rays with barium enema [85]. Paul Schumacher, in 1929, confirmed these findings by X-rays with IV glucose administration [86]. Baer et al. [87] showed by barium enema that the growing uterus progressively displaces the appendix out of the pelvis after the third month, into the upper right quadrant, by as much as two fingerbreadths above McBurney's point, with a counterclockwise rotation of the tip (Fig. 15.7). The appendix returns to its normal position by postpartum day 10. The original description by Charles Heber McBurney is that pressure is applied by one finger “exactly between 1½ and 2 inches from the anterior spinous process of the ileum on a straight line drawn from that process to the umbilicus.” This landmark corresponds to the areas of the inflamed appendix irritating the abdominal peritoneum over the T11 and T12 dermatomes. The pain and hyperesthesia



**Fig. 15.7** Change of the location of the appendix during pregnancy according to Baer et al. [87]. (Springer illustration from second edition of *Acute Abdomen During Pregnancy*)

are present over McBurney's point despite the possible upward displacement of the appendix [88]. Others did not confirm the upper displacement of the appendix using physical examination, imaging techniques, or intraoperatively [26, 85, 89–93]. Positional changes may be hampered by adhesions that restrict the free movement of the appendix, especially the retrocecal (subserosal) position. Hodjati and Kazerooni found a significant positional change ( $>2$  cm) of the appendix in 15–23% [92]. This discrepancy is partly due to the different extents of cecal fixation. MRI studies confirmed the upward displacement of the appendix in the term pregnant woman [94, 95].

A growing pregnant uterus could displace a mobile cecum with the appendix. (Partly) fixed cecum or retrocecal (subserosal) appendix cannot be displaced.

The most challenging interpretation of abdominal pain is immediately before, during, and immediately after the labor. With uterine contractions before labor, AA is likely when severe abdominal pain remains between contractions or persists after delivery [50].

*Abdominal pain aggravated by fetal movements* is sometimes detected [55, 96, 97]. One of the first mentions of this symptom was by Emil Jerlov in 1929 [95], William Marbury in 1933 [98], and Urban Maes in 1934 [55].

*Nausea* is nearly always present, and vomiting in 70–87% of patients [93]. These symptoms are exaggerated due to the following: (1) progesterone-induced delayed gastric emptying and (2) pressure of the enlarged uterus on the hollow viscus. Symptoms could be misleading because many women with normal pregnancies have these symptoms, especially in early pregnancy [29]. AA is likely with new-onset nausea (the period of nausea and vomiting in early pregnancy is primarily self-limiting and confined to the first trimester).

*Anorexia* is present in 1/3 to 2/3 of pregnant while almost universal in nonpregnant patients [19, 20, 99]. New-onset anorexia should raise suspicion, especially with other symptoms and signs suggestive of AA.

*An atypical clinical picture* is most common in the second trimester [24]. RUQ pain (12%), uterine contractions, dysuria (20%), and diarrhea could mask AA [26, 28, 46, 80].

In pregnancy with obstetric complications, such as *miscarriage* [53] or *preterm labor* [100–102], and abdominal or pelvic pathology symptoms, AA should be excluded first, which could cause these obstetric complications. Obstetric complications from AA in pregnancy were pointed out in the nineteenth century [103–105].

### 15.5.2 Physical Examination

The abdominal wall changes during pregnancy, with muscle tone reduction and skin elasticity to accommodate the enlarging uterus. The abdominal wall tone remains lax for several weeks postpartum, returning to a near-nonparous level in 6–7 weeks. The chronic stretching of the parietal



peritoneum by the growing uterus, particularly in the third trimester, decreases the number of afferent sensory nerve fibers of the peritoneum per square. A high circulatory level of adrenocorticoids in pregnancy diminishes the tissue response to inflammation, masks the early signs of infection, and hinders localization. Increased parietal and visceral peritoneum separation by an enlarging uterus causes decreased perception and localization of somatic pain. These changes make clinical localization of inflamed appendix unreliable.

The hallmarks of acute surgical disease, abdominal guarding, and rigidity do not occur or are attenuated during the early puerperium. This is responsible for the delay in proper diagnosis.

There is no single and reliable sign for the diagnosis of AA in pregnancy. Some classic signs of AA, such as Rovsing's or Psoas' sign, have no diagnostic value for AA in pregnancy [28].

An *abdominal mass* may be missed on physical examination because of the enlarged gravid uterus [106].

On direct palpation, abdominal tenderness in the RLQ is always present [80, 93, 107].

*Rebound tenderness* is present in 55–93% [25, 80, 93, 99, 108, 109] and *abdominal muscle rigidity* in 50–65% [25, 44]. These two signs are more common during the first trimester. In the second and the third trimesters, as the abdominal wall distends, the anterior abdominal wall is distanced from the inflamed appendix losing the ability to elicit guarding and rigidity [46, 110].

*Rovsing's sign* is variable, present in 18–60% [21, 25, 109, 111], while trimester distribution is unknown. A positive sign in the third trimester could be due to the separation of the abdominal wall from the colon, without the possibility of its compression.

*The psoas's sign (Obraztsova's sign)* is less frequent during pregnancy (5–50% [109, 112]) compared to nonpregnant patients with AA [19].

*Obturator's sign* is found in 21% of patients [109].

*Rectal or pelvic tenderness* may occur in early pregnancy but is unusual in late pregnancy as the appendix is dislodged from its pelvic location and shielded by the enlarged uterus [109, 113]. Therefore, <50% had tenderness on rectal examination [108, 109].

*Alders' sign* can differentiate AA from tubo-ovarian pathology with RLQ pain in pregnancy and puerperium [114]. The point of maximal tenderness is determined while the patient is supine. Then, roll the patient onto the left side. If pain shifts toward the center, then it may be tubo-ovarian. The problem in pregnant patients in the third trimester is that the enlarged uterus does not allow the tubo-ovarian complex to shift its position. This sign is helpful if the uterus is not large enough to be palpable abdominally. It may be misleading when a uterine lesion has become fixed by adhesions to the anterior abdominal wall. In acute salpingitis, the result will depend on the presence or absence of perisalpingitic adhesions. Approximately 36% of patients with proven AA had positive Alders' sign [109] without comparing trimesters.

*Aaron's sign* is a referred pain or discomfort in the precordial or epigastric region when continuous firm pressure is applied over McBurney's point [115].

*Bryan's sign* is abdominal pain produced by shifting the gravid uterus to the right; by some, the most reliable sign [116].

The *mean maximal axillar temperature* is 37.2–37.9 °C but could be >39 °C with perforation and diffuse peritonitis [17, 69, 93]. Approximately 50–70% of pregnant patients with AA have a low-grade fever [25, 93, 108, 117]. This incidence of elevated temperature is not different from the normal pregnant population, the finding is also true for *tachycardia* [45, 117], and both are not sensitive signs [26, 118], predicting only perforation and peritonitis. Pregnant patients with low-grade fever also have leukocytosis, complicating the definitive diagnosis [93].

# 15.6 Differential Diagnosis

Differential diagnosis is more extensive than in nonpregnant patients due to the following:

- Less reliable history and physical examination,
- Higher incidence of additional conditions that mimic AA.

These conditions are presented as non-obstetric/nongynecologic and gynecologic/obstetric conditions (Table 15.3).

## 15.6.1 Round Ligament Pain/Syndrome

Round ligament pain or syndrome (RLP) is one of the most common abdominal discomforts of pregnancy and usually starts in the second trimester of gestation and continues until delivery. It usually resolves entirely after delivery or early postpartum. The most common symptoms are sudden pain in the lower abdomen, usually on the right side of the pelvic area that can extend to the groin, and shooting abdominal pain during sudden movements or physical exercise. Pain is sudden and intermittent and lasts a few seconds. The

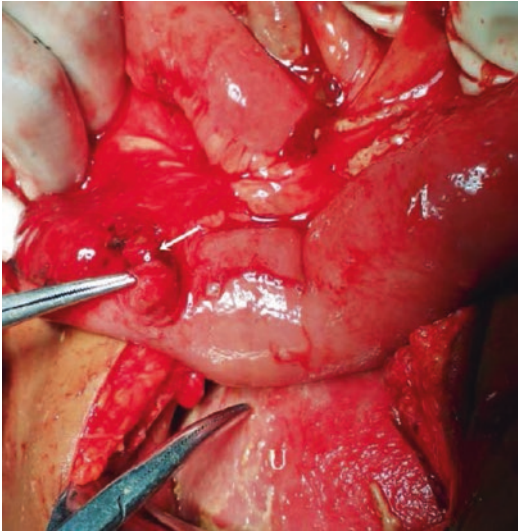
most common causes are as follows: (1) *round ligament spasm or cramp* when the ligament contracts involuntarily. The ligament pulls on the female reproductive system's nerve fibers and sensitive structures. Since the uterus tends to rotate to the right, the pain is often right-sided, leading to confusion with AA [119]; (2) the increase in size and weight of the uterus puts stress on the ligament that holds it, causing *round ligament stretching* (see Sect. 19.1.5.2); (3) *round ligament varicosities*—enlargement of the blood vessels of the round ligament, can occur during pregnancy, causing pain and swelling (see Sect. 19.1.5.1); (4) *round ligament/inguinal endometriosis* (see Sect. 19.1.5.3); and (5) other pathologies of uterine round ligament causing RLP. However, the diagnosis of RLP is one of exclusion (see Sect. 19.1.5).

## 15.6.2 Meckel's Diverticulitis

Symptomatic Meckel's diverticulum/diverticulitis (MD) during pregnancy is exceptionally rare (Fig. 15.8). Wenzl, in 1949, published the first case of MD in pregnancy [121]. Approximately 40 cases of MD complicating pregnancy have been reported since 1949 [122, 123]. The average maternal age in symptomatic MD is rising—until

**Table 15.3** Differential diagnosis of acute appendicitis during pregnancy and puerperium

| Non-obstetric/nongynecologic conditions | Gynecologic/obstetric conditions  |
|-----------------------------------------|-----------------------------------|
| Gastroenteritis                         | Ruptured/hemorrhagic ovarian cyst |
| Urinary tract infections                | Adnexal torsion                   |
| Pyelonephritis                          | Salpingitis                       |
| Nephrolithiasis                         | Tubo-ovarian abscess              |
| Acute cholecystitis                     | Threatened abortion               |
| Acute pancreatitis                      | Placental abruption               |
| (incarcerated) hernia                   | Chorioamnionitis                  |
| Bowel obstruction                       | Pelvic inflammatory disease       |
| Cecal carcinoma                         | Degenerative fibroid              |
| Mesenteric adenitis                     | Ectopic pregnancy                 |
| Spontaneous rectus hematoma             | Preeclampsia                      |
| Pulmonary embolism                      | Round ligament syndrome/pain      |
| Right lower lobe pneumonia              | Varicose veins in the parametria  |
| Meckel's diverticulitis                 | Preterm labor                     |
| Sickle cell disease                     | Pelvic endometriosis              |
| Stump appendicitis                      | Metritis                          |
| Inflammatory bowel disease              | Ovarian vein syndrome             |



**Fig. 15.8** Meckel's diverticulum at the antimesenteric border of the ileum with a perforation at the tip (*white arrow*). Gravid uterus (*U*). (Reproduced with permission from [120])

1990, it was 24 years (range 17–31) [123], and after 1990 it raised to 27 [14–34, 38] [122], probably due to increasing maternal age during pregnancy. It is rare during the first trimester and equally frequent (48%) in the second and third trimesters [122].

Presenting symptoms include abdominal pain (88.9%), nausea or vomiting (59.3%), fever (18.5%), abdominal distension (18.5%), hematochezia (11.1%), constipation (11.1%), hematemesis (3.7%), diarrhea (3.7%) and asymptomatic (3.7%) [122]. The most common type of MD presentation is perforation (40–57%) [122, 124], with an equal incidence of intussusception, bleeding, inflammation, and small bowel obstruction (11.1%) [122]. In the nonpregnant adult population, MD perforation occurs in 7.3–26.8% [125–127]. In the general population, bleeding is the most common presentation in patients younger than 20 years [128, 129] and is rare beyond 30.

MD perforation is more common during pregnancy than in the general adult population.



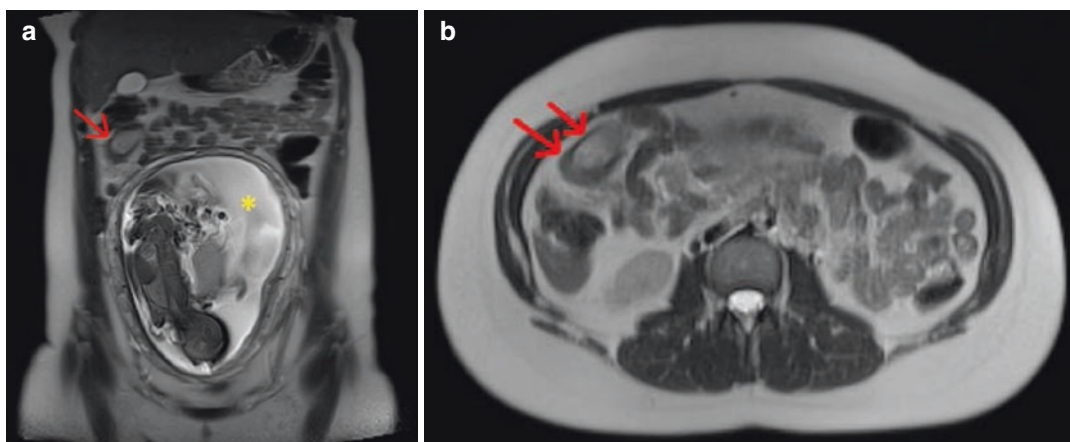
**Fig. 15.9** Abdominal CT shows 6.0 × 4.7 cm rim-enhancing fluid collection with extraluminal air in the right iliac fossa surrounded by collapsed small bowel loops. Dilated, fluid-filled small bowel loops in the left lower abdomen indicate small bowel obstruction with a transition point at the ileal level. (Reproduced with permission from [123])

Before the era of CT and MRI, preoperative diagnosis is challenging (9% until 2002 [124] and 7.4% until 2021 [122]). Diagnostic imaging modalities utilized after 1990 were abdominal US (40.7%), CT (25.9%), MRI (14.8%), plain abdominal X-ray (11.1%), and endoscopy (7.4%). No cases utilized scintigraphy [122]. Even if detected, it mimics AA on the transabdominal US as a noncompressible tubular structure (see Sect. 15.7.3). Although their accuracy is low, CT and MRI can distinguish between AA and MD in pregnancy [122]. CT can define the pathophysiologic process causing MD (Fig. 15.18) or indirect signs, such as small bowel obstruction (Fig. 15.9). MRI can reveal a thick-walled hollow structure emanating from the distal ileum with infiltrative changes, suggesting an inflammation (Fig. 15.10).

Treatment follows the principles of incidental MD in pregnancy (see Sect. 15.9.2).

### 15.6.3 Crohn's Disease

See Chap. 21.



**Fig. 15.10** (a) Coronal MRI image shows inflamed Meckel's diverticulum (red arrow) and gravid uterus (yellow star). (b) Axial MRI image shows inflamed Meckel's diverticulum (arrows). (Reproduced with permission from [131])

#### 15.6.4 Urolithiasis/Urinary Tract Infection

John Osborn Polak (March 12, 1870—June 29, 1931), in 1929, described the difference in the sequence of events between AA and pyelitis [132], which is diagnostic. With AA, the pain could be followed by fever and rarely chills. With pyelitis, chills come first, then fever and pain (see Sect. 27.3.4).

#### 15.6.5 Vomiting of Pregnancy

In 1905, Heaton explained the difference between AA and vomiting of pregnancy. *The illness may be of all degrees of severity, from the transient appendiceal colic to the fulminating AA, which proves fatal in a few hours. In the mild cases, the sickness which ushers in the illness is liable to be mistaken by both patient and practitioner for the ordinary vomiting of pregnancy. The use of the clinical thermometer in a doubtful case should prevent mistake, for the vomiting of pregnancy is “apyrexial,” and the presence of fever, however slight, should always put us on our guard and lead us to make a careful examination of the right iliac region* [53]. Unfortunately, low-

grade fever is present in 50% of patients with AA (see Sect. 15.5.2).

#### 15.6.6 Fitz-Hugh-Curtis Syndrome

Perihepatitis (Fitz-Hugh-Curtis syndrome) results from early bacteremia or retroperitoneal lymphatic dissemination of *C. trachomatis* or gonococcal pelvic infection [133]. The syndrome is most frequent in young women and more common in the second and third trimesters and puerperium. Inflammation in the RUQ produces perihepatic adhesions. Classically, there is a sudden onset of sharp RUQ pain, often pleuritic in quality. Nausea and hiccups are occasional. Physical findings include RUQ tenderness, an occasional hepatic friction rub, and fever. Pelvic examination may be normal or reveal signs of cervicitis or pelvic inflammatory disease. Liver function tests may be transiently abnormal. A history of recent pelvic infection suggests the diagnosis, but the syndrome can be a sequel of latent or asymptomatic infection. The diagnosis is further supported by the isolation of gonococcus on cervical culture and the improvement from appropriate antibiotics [133]. Other conditions should be excluded because specific diagnostic markers are lacking.

## 15.6.7 Puerperium-Associated Diseases

### 15.6.7.1 Metritis

The most common of these is *metritis*, the broad group of postpartum infections of the genital tract. Metritis is often insidious in onset. Because of the vague initial manifestations, it is often a diagnosis of exclusion. Endometritis, or deciduitis, is an infection of the most superficial layer of the uterus and is the most common site of puerperal infection. Endometritis onset is commonly 2–5 days postpartum, and the earliest manifestations are malaise, anorexia, and fever. There may be no localizing signs or symptoms in mild cases. The pelvic examination may be normal, even in severe endometritis. The disease may progress further to involve the myometrium (myometritis) and parametrial structures (parametritis) with extension into the broad ligaments, tubes, ovaries, and pelvic peritoneum [79]. When the parametria are involved, pain and tenderness are present deep in the groin. Extensive infection may produce lethargy, chills, high fever, and significant lower abdominal pain, tenderness, and rebound. Accompanying paralytic ileus may cause distention and vomiting. Myometritis and parametritis are usually accompanied by cervical motion tenderness and localized peritoneal signs, rarely generalized peritonitis. The lochia may provide a clue as to the true nature of the difficulty. Within 48 h, the lochia of endometritis becomes serous, seropurulent, or foul-smelling if the infection is saprophytic. A flare-up of gonorrheal salpingitis seldom begins before the seventh day, and the findings usually are limited to the pelvis. A positive history of the previous infection is important for the diagnosis.

### 15.6.7.2 Pelvic Thrombophlebitis/Ovarian Vein Syndrome

Thrombophlebitis and thromboembolic events are more common in pregnancy, especially puerperium. Ovarian vein thrombosis (syndrome) complicates <0.05% vaginal deliveries and 1–2% Cesarean sections (CS) [134]. Ovarian vein thrombosis involves the right ovarian vein in

90%. It is attributed to retrograde flow in the left ovarian vein and antegrade flow in the right ovarian vein in the postpartum period. This difference in blood flow may be attributable to the physiologic dextrorotation of the uterus during pregnancy and compression of the right ovarian vein. Puerperium predisposes to deep vein thrombosis attributable to sluggish circulation, trauma to the pelvic vessels during delivery, immobilization, and estrogen-mediated hypercoagulability.

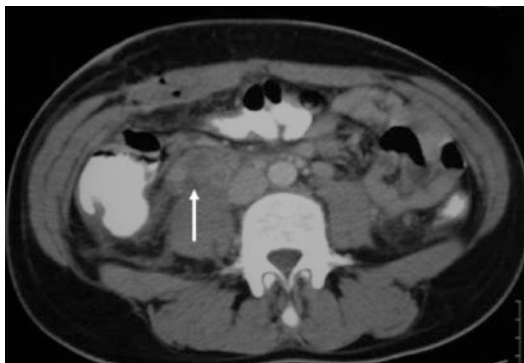
Other risk factors include abortions, gynecological surgery, malignancy, pelvic inflammatory disease, Crohn's disease, and infections with *Campylobacter fetus* and group A streptococcal bacteremia. Inherited thrombophilia, primarily factor V Leiden mutations and protein S deficiency, has been reported in 50% of patients with ovarian vein thrombosis. There are cases of ovarian vein thrombosis associated with antiphospholipid syndrome and heparin-induced thrombocytopenia-type II.

Pelvic thrombophlebitis, or right ovarian vein syndrome, commonly presents with abdominal/pelvic pain (66%), fever (80%), and a tender midabdominal or RLQ mass [134]. However, the diagnosis is often complicated by other nonspecific symptoms and signs: back pain, nausea, vomiting, tachypnea, tachycardia, hypotension, ileus, and sepsis [135]. It may be difficult to distinguish from metritis but should be considered after a poor response to appropriate antibiotics or exclusion of adnexal torsion (see Sect. 6.6). Diagnosis can be delayed due to fever and elevated laboratory inflammatory markers that mislead the diagnosis of AA, urinary tract infection, or tubo-ovarian abscess [136].

The diagnosis is frequently made after a fever is nonresponsive to antibiotics for 48 h. Color Doppler US is the first diagnostic procedure [137], but due to low sensitivity and high false negative and false positive rates, IV contrast-enhanced CT is preferred. The sensitivity (Fig. 15.11) is 100% compared to 92% with gadolinium-enhanced MRI and 50% of duplex color Doppler US [139].

Untreated postpartum ovarian vein thrombosis carries the risk of severe complications like sep-





**Fig. 15.11** Abdominal CT shows thrombosed right ovarian vein (arrow). (Reproduced with permission from [138] under the CC BY 2.0)

sis and extension into the inferior vena cava. Septic pulmonary embolism occurs in 11–33%, with a mortality of 4–5% [140]. Successful treatment includes anticoagulation for 3–6 months with low molecular weight heparin and antibiotics for 2 weeks. Surgical treatment is reserved when (1) anticoagulation is contraindicated, (2) treatment-related complications occur, and (3) with a high risk for pulmonary embolism—free-floating thrombus, an extension of thrombus, or recurrent pulmonary embolism despite adequate medical therapy [141, 142]. Surgical interventions include ligation and splitting the thrombosed ovarian vein and inferior vena cava or placement of inferior vena cava filters to prevent pulmonary embolism.

No uniform guidelines exist for the evaluation of thrombophilia after ovarian vein thrombosis. Pregnancy and the puerperium are hypercoagulable states, with a predisposition to ovarian vein thrombosis. The risk factors associated with postpartum ovarian vein thrombosis include several thrombophilias—antiphospholipid syndrome, lupus anticoagulant, factor V Leiden mutation, MTFHR C677T deficiency, and protein S deficiency [143]. However, the *American College of Obstetricians and Gynecologists* recommends testing white women with a previous deep vein thrombosis for the factor V Leiden mutation and individualizing testing in nonwhite women [144].

## 15.7 Diagnosis

*Medicine is a science of uncertainty and an art of probability.*

(Sir William Osler)

*The diagnosis of acute appendicitis is more difficult than at other times, as the enlarged uterus renders it almost impossible to explore the right iliac region satisfactorily.*

(John Whitridge Williams, 1903)

Diagnostic workup should be done in a hospital in cooperation with the obstetrician. No significant difference in the median time from presentation to first imaging or surgery, the incidence of negative pathology, or appendiceal rupture exists between women who presented to the ED or obstetrics triage [145]. The lag time between arrival to the ED and laparotomy was significantly higher in the second half of pregnancy than in the first half (11.6 vs. 7.7 h, respectively) [37].

### 15.7.1 Laboratory Findings

A pregnant woman's physiologic leukocytosis, increased heart rate, and respiratory alkalosis make her more likely to meet systemic inflammatory response syndrome criteria than a nonpregnant woman [146].

*Leukocytosis* (raised white blood cell count—WBC) is not diagnostic due to the physiologic rise in pregnancy, reaching 20,000/mm<sup>3</sup> in early labor [147]. Despite that, a pregnant patient undergoing appendectomy has an average WBC value of over 13,000/mm<sup>3</sup> compared to 10,500/mm<sup>3</sup> of healthy pregnant women [148–150]. The values over 16,000/mm<sup>3</sup> are highly suspicious [21, 26, 44, 118, 151] and also indicate appendiceal perforation [109]. Only 60% with perforation had WBC >16,000/mm<sup>3</sup> [29]. Different WBC cutoff values had different sensitivities and specificities for AA [150]. With suspected AA and normal WBC levels, serial (every 6 h) WBC measurements [152, 153] or a comparison with previous WBC values during normal pregnancy is helpful. If WBC values during previous

normal pregnancy were within normal limits, then RLQ pain with elevated WBC is a predictor of AA.

*Neutrophil granulocytosis with the left shift* implies acute bacterial infection. Without the left shift, granulocytosis >80% should raise suspicion of AA [93]. Even normal values are found with AA in pregnancy [26, 154]. *Neutrophil-to-lymphocyte ratio* (NLR) values are significantly higher in AA patients than in healthy pregnant women and pregnant women under acute abdominal observation [150]. Cutoff values differ from 5.5 to 6.84, resulting in different sensitivities and specificities in most scenarios >80% [148, 150, 155].

A *C-reactive protein* (CRP) is normal during pregnancy and delivery. After delivery of normal pregnancy, values increase 10–20-fold (never >10 mg/L) compared to levels at admission. Pregnant patients with gestational diabetes, diabetes mellitus, obesity, or pregnancy-induced hypertension have maximal CRP levels of 10 mg/L [156–159] even despite racial differences [160]. CRP starts to increase within 8–12 h as a response to inflammation. Its increase is slower than that of WBC and reaches a maximum level within 24–48 h. Interestingly, positive cases had negative CRP values when evaluated <12 h from the onset of pain [118]. Sixty-eight percent with AA had CRP  $\pm$  10 mg/L, but all patients with perforation had elevated CRP (mean 55 mg/L) [29]. CRP value increases while the albumin level decreases in the acute phase response secondary to inflammation in pregnant patients. *CRP-to-albumin ratio* (CAR) was significantly higher in patients who underwent appendectomy after AA diagnosis than in pregnant women under acute abdominal observation or healthy pregnant women [150]. Also, the number of lymphocytes was lower, but CRP was higher in AA patients than in healthy pregnant women. The number of lymphocytes decreased while the CRP value increased depending on the severity of the infection [148, 150, 155]. Lymphocyte-to CRP ratio (LCR) is significantly lower in a patient with AA than in healthy pregnant women [150].

Elevated WBC, NLR CRP, CAR, and LCR levels could be used as supportive parameters for physical examination and anamnesis for AA diagnosis in pregnant patients [150].

The *erythrocyte sedimentation rate* is physiologically elevated and less reliable monitoring of inflammatory activity during pregnancy [161].

*Leukocyturia* (57%) and *bacteriuria* (41%) are common with AA [80]. This may represent concurrent asymptomatic (or symptomatic) bacteriuria, frequent in pregnancy [19]. Other abnormalities such as *mild proteinuria* or *hematuria* are present in up to 19% of pregnant patients [108].

Puerperal changes in blood components may be confusing as well. During the first 10–14 days of the puerperium, WBC counts of 20,000–25,000/mm<sup>3</sup> are not unusual; there is also a predominant increase in neutrophils. The erythrocyte sedimentation rate may increase to 50–60 mm/h. Reliance on the erythrocyte sedimentation rate or the WBC count for diagnosing acute infection may be misleading [79].

## 15.7.2 Diagnostic Scoring Systems

Isolated clinical signs and blood indices are unreliable for diagnosing AA in pregnancy and lead to an unacceptable negative appendectomy rate (NAR), up to 50%, without imaging [37]. Therefore, clinical imaging scoring systems have been developed to diagnose AA in the nonpregnant population accurately.

### 15.7.2.1 Alvarado Score and Modifications

The most common score in the general population is the *Alvarado score* (AS) [162]. The mnemonic is MANTRELS (Table 15.4). AS sensitivity (54.0–96.2%) and specificity (54.0–74.3%) vary significantly. AS [163–165] and *modified AS for pregnant patients* [166] have

**Table 15.4** Comparison of Alvarado score and modified Alvarado score for pregnant patients

| <i>Alvarado Score</i>                                                                 |           | <i>Modified AS for pregnant patients</i>                                              |          |
|---------------------------------------------------------------------------------------|-----------|---------------------------------------------------------------------------------------|----------|
| Symptoms                                                                              | Score     | Symptoms                                                                              | Score    |
| Migratory RLQ pain                                                                    | 1         | RLQ pain                                                                              | 2        |
| Anorexia                                                                              | 1         | Anorexia                                                                              | 1        |
| Nausea/vomiting                                                                       | 1         | Nausea/vomiting                                                                       | 1        |
| <i>Signs</i>                                                                          |           | <i>Signs</i>                                                                          |          |
| Tenderness in RLQ                                                                     | 2         | Tenderness in RLQ                                                                     | 2        |
| Rebound tenderness in RLQ                                                             | 1         | Rebound tenderness in RLQ                                                             | 1        |
| Elevated temperature<br>( $\geq 37.3^{\circ}\text{C}$ / $\geq 99.1^{\circ}\text{F}$ ) | 1         | Elevated temperature<br>( $\geq 37.3^{\circ}\text{C}$ / $\geq 99.1^{\circ}\text{F}$ ) | 1        |
| <i>Laboratory</i>                                                                     |           | <i>Laboratory</i>                                                                     |          |
| Leukocytosis ( $>10,000/\text{mm}^3$ )                                                | 2         | Leukocytosis ( $>10,000/\text{mm}^3$ )                                                | 1        |
| Shift to the left ( $>75\%$ )                                                         | 1         |                                                                                       |          |
| <b>Total score</b>                                                                    | <b>10</b> | <b>Total score</b>                                                                    | <b>9</b> |

**Table 15.5** Alvarado score with confirmed acute appendicitis in pregnant (by trimesters) and nonpregnant

| Statistical method | Pregnant (%) |        |       |       |                 |
|--------------------|--------------|--------|-------|-------|-----------------|
|                    | Trimester    |        |       |       |                 |
|                    | First        | Second | Third | Total | Nonpregnant (%) |
| Sensitivity        | 93           | 65     | 75    | 79    | 73              |
| Specificity        | 50           | 83     | 75    | 80    | 75              |
| PPD                | 93           | 92     | 75    | 94    | 94              |
| NPD                | 7            | 35     | 75    | 21    | 13              |
| Accuracy           | 88           | 70     | 75    | 79    | 74              |

Reproduced with permission from [164]

PPD positive predictive value, NPD negative predictive value

been tested in the pregnant population. The difference in comparison to the standard AS is that migration of pain is not included. Also, the number of points for pain in RLQ is 2 compared to 1 point in the standard AS for the nonpregnant population. Leukocyte left shift is not included, and leukocytosis (which could be present in a normal pregnancy) has only 1 point in *modified AS for pregnant patients*. The total score is lower by 1 point (9 vs. 10) (Table 15.4). The positive predictive value was 60% with AS 5–7 and 100% with AS 7–9. The sensitivity and specificity of AS 7 are 80% [163–165].

The AS can be falsely higher in pregnancy due to physiologic leucocytosis in the late pregnancy and a higher frequency of nausea and vomiting during the first trimester [164, 165]. Also, the pain localization in the RLQ and the pain migration might vary due to the growth of the uterus leading to different AS values in pregnancy [164, 165]. The specificity and sensitivity according to the trimesters are presented in Table 15.5.

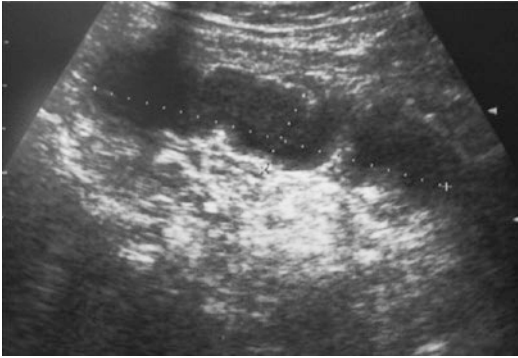
### 15.7.3 Transabdominal Ultrasound

The *American College of Radiology Appropriateness Criteria* recommends it as the initial imaging modality for suspected AA in pregnancy [167]. Most patients are submitted to the abdominal US preoperatively [17, 168]. Apart from identifying underlying pathology, it can identify cervical incompetence [169], obstetric complications (see Sect. 15.10.4), and fetal status. US criteria are the same as in the nonpregnant population for the diagnosis of AA [170] as follows:

- Noncompressible appendix,
- Appendiceal diameter  $>6$  mm,
- Appendiceal wall thickness  $\geq 2$  mm,
- Free fluid around the appendix,
- Complex mass in the area of the appendix.

Indirect signs include abnormal fluid collections in the pelvic cavity or around the cecum/appendix. Evaluation of the entire appendiceal length may be challenging with an enlarged gravid uterus, and the focal area of AA may be missed. In many instances, AA is morphologically evident only on its tip, which is sometimes not visualized [170].

Sensitivities vary dramatically, 18–100% with higher specificities, 80–100% [22, 80, 93, 148, 161, 168, 170–176]. The positive predictive value is near 100%. The differentiation between MD and AA can be difficult because both are non-compressible tubular structures in RLQ (Fig. 15.12).



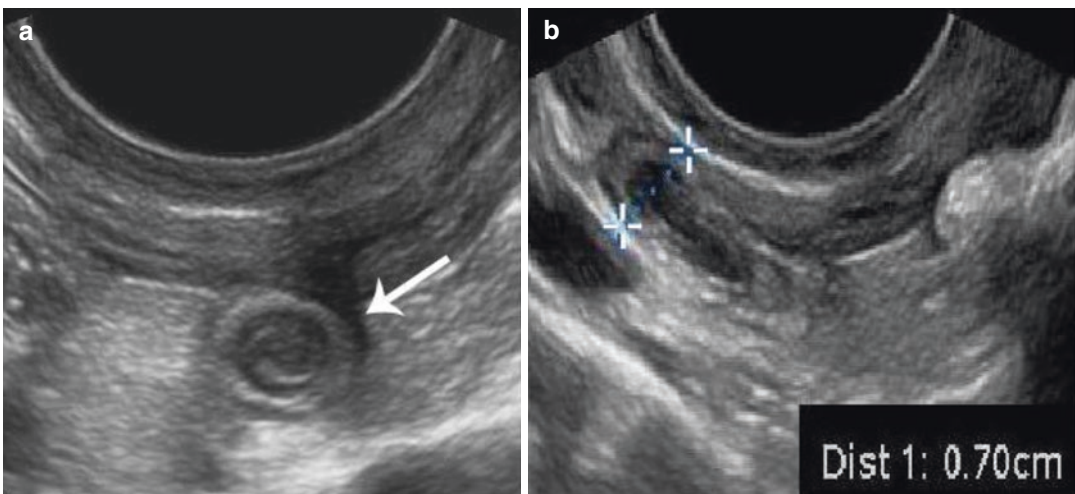
**Fig. 15.12** Transabdominal sonogram shows a tubular cystic structure, 8 × 2 cm in the right iliac fossa, found to be giant Meckel's diverticulitis. (Reproduced with permission from [177])

The accuracy of transabdominal US in a supine position during late pregnancy is challenging because the enlarged gravid uterus prevents graded compression. In the second half of pregnancy, the patient should be placed in the left posterior oblique or left lateral decubitus position, allowing displacement of an enlarged uterus allowing the graded compression US technique [171]. High clinical suspicion with a normal or inconclusive transabdominal US indicates an abdominal MRI or CT [168].

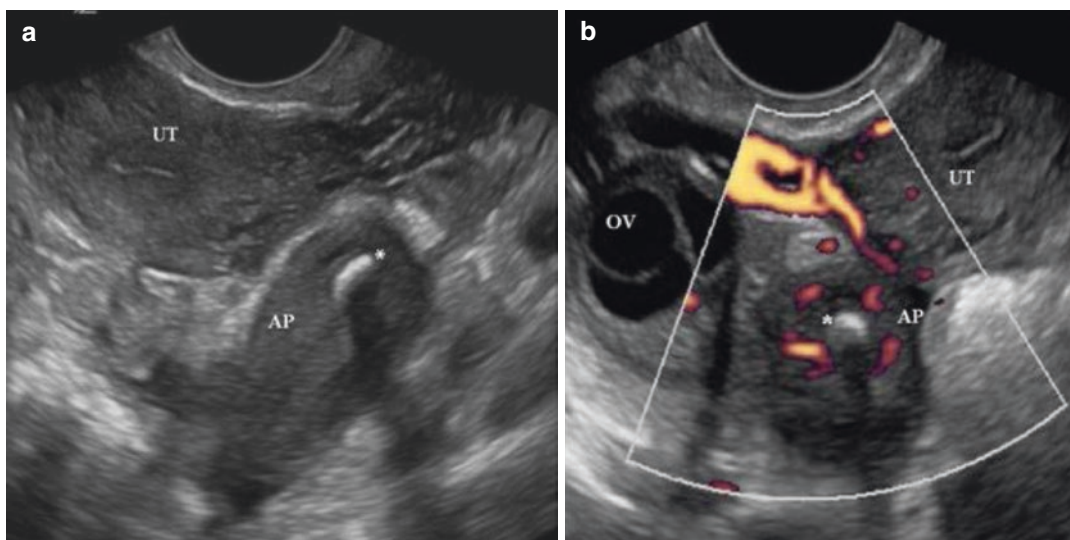
### 15.7.4 Transvaginal Ultrasound

There are no *Royal College of Obstetricians and Gynaecologists* guidelines about the use of transvaginal US. The transvaginal US can detect the following [178]:

- Presence and size of adnexal or uterine pathology ruling out AA,
- Free fluid in the pouch of Douglas,
- Pathology in the ileocecal region (cecal tumors, cecal diverticula, or retroperitoneal tumors),
- AA (aperistaltic, tubular structure measuring  $\geq 6$  mm; hyperemia; appendicolith; free fluid around the appendix) (Figs. 15.13 and 15.14).



**Fig. 15.13** Transvaginal imaging of the right adnexa. (a) Transverse view of the appendix. (b) Long view of the appendix measuring 0.7 cm. (Reproduced with permission from [179] under the CC BY 3.0)



**Fig. 15.14** Transvaginal imaging of the right adnexa demonstrating appendicitis. (a) Enlarged appendix (AP) with appendicolith (\*). The uterus (UT) is also seen. (b) Hyperemic

appendix (AP) visualized in transverse, appendicolith (\*), right ovary (OV), and uterus (UT) seen. (Reproduced with permission from [179] under the CC BY 3.0)

Apart from identifying underlying pathology, it can identify cervical incompetence [169] and other obstetric complications (see Sect. 15.10.4).

Transvaginal Doppler US defines adnexal torsion or vascularized tumors. In nonpregnant women, 24% with AA were diagnosed by the transvaginal US after negative transabdominal US [178]. Some recommend transvaginal US as the first US diagnostic tool for female patients with low abdominal pain [179].

### 15.7.5 Abdominal MRI

After the indeterminate US, the *European Society of Urogenital Radiology* [180] and the *American College of Radiology* [181] recommend abdominal MRI or CT when MRI is unavailable. Therefore, indications for abdominal MRI are as follows:

- The appendix not visualized by abdominal US,
- No other cause of abdominal pain on US.

The MRI criteria for AA include (Fig. 15.15) the following:

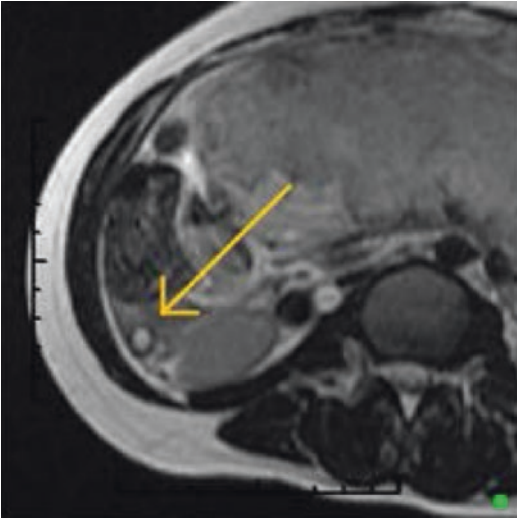
- Appendiceal diameter >7 mm,
- Appendiceal wall thickening >2 mm,
- Fluid-filled appendix,
- Appendicolith,
- Periapendicular inflammation (periapendicular fat stranding and fluid),

The MRI criteria that exclude AA are (1) appendiceal diameter <6 mm or (2) appendiceal diameter of 6–7 mm with no evidence of periappendicitis (Fig. 15.16). The second MRI scenario warrants close clinical follow-up.

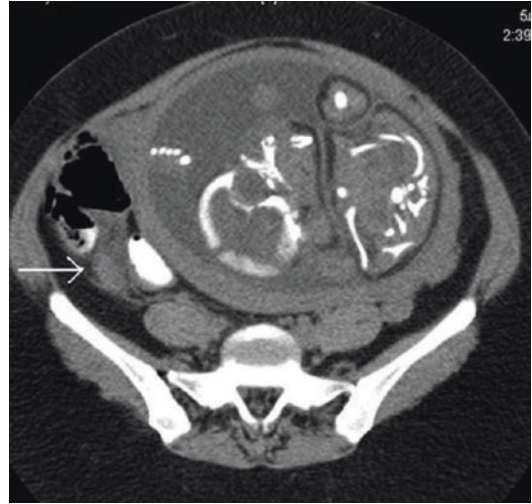
MRI has high sensitivity (91.8%) and specificity (97.9%) for AA in pregnant patients [183]. Advantages of MRI for suspected AA in pregnancy include the following:

- Reduced rates of both negative laparotomy and perforation [184–186],
- Identification of other causes of abdominal pain [185–188],
- More frequent discharge from the emergency department [184],

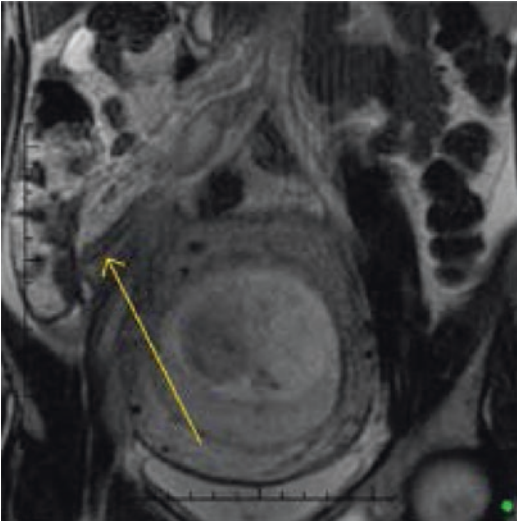




**Fig. 15.15** Axial T2-weighted image shows dilated appendix (*arrow*) consistent with acute appendicitis. (Reproduced with permission from [182])



**Fig. 15.17** Transverse section of an oral and IV contrast-enhanced CT shows a thickened appendix and periappendicular fat stranding (*arrow*) in 27 weeks of pregnancy, confirming acute appendicitis. (Reproduced with permission from [189])



**Fig. 15.16** Coronal T2-weighted image shows normal appendix (*arrow*) at 14 weeks gestation. (Reproduced with permission from [182])

- Shortened length of stay in non-operated and operated groups [184, 186],
- Identification of cervical incompetence [169].

Except for diagnosing AA, MRI accurately detects the degree of AA inflammation for non-

operative treatment (see Sect. 15.8.1). After the inconclusive US, abdominal MRI did not lower the AA perforation rate [186].

### 15.7.6 Abdominal CT

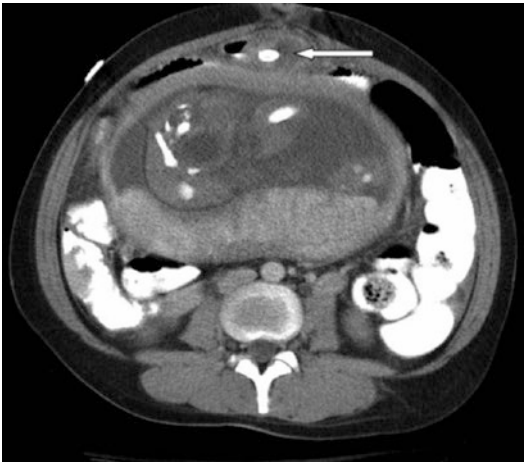
CT of the appendix is positive for AA with the following (Fig. 15.17):

- Enlarged appendix (maximum diameter >6 mm),
- Periappendiceal inflammatory changes (fat stranding, phlegmon, fluid collection, and extraluminal gas).

In a pregnant population with AA, sensitivity and specificity are similar to the general population, over 90% [189–191]. CT established a diagnosis in 30% of cases with an initial negative US [191]. The higher the degree of appendiceal inflammation, the higher the sensitivity for detecting AA in pregnancy [192]. Abdominal CT delineates other condi-

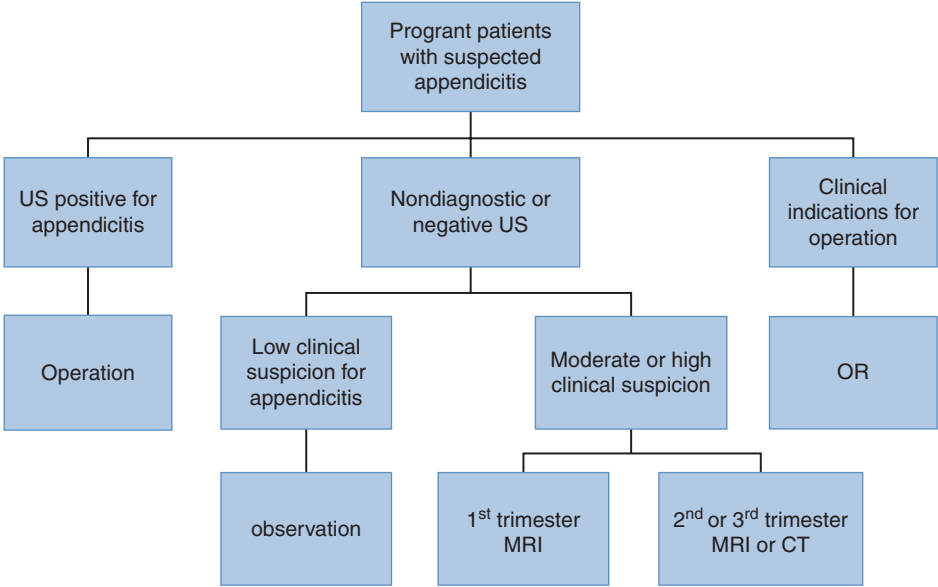
tions with the clinical presentation of AA, such as MD (Fig. 15.18). A low-dose (<2.5 mGy) protocol is sufficient to confirm or rule out AA in 83% [193]. Standard-dose CT or MRI can reveal the diagnosis of the remaining cases.

For diagnosing AA in pregnancy, a low-dose abdominal CT should be used for an uncertain clinical diagnosis, equivocal laboratory or US findings, or limited access to MRI or MRI expertise.



**Fig. 15.18** Contrast-enhanced abdominal CT shows an intrauterine pregnancy of 29 weeks with a fluid-filled collection under the umbilicus containing an enterolith. (Reproduced with permission from [130])

The simplified diagnostic algorithm is presented in Fig. 15.19.



**Fig. 15.19** Algorithm for the evaluation of pregnant patients with suspected acute appendicitis. (Reproduced with permission from [176])

## 15.8 Treatment

*In these cases, the usually conservative surgeons of Germany take, as a rule, the same radical stand which is taken by their American and French colleagues.*

(Howard Atwood Kelly, 1909)

*In case of a relapse in a pregnancy, the operation is to be recommended even while the clinical symptoms are of a mild nature, especially in the earlier months of the pregnancy.*

(Fränkel)

*If appendicitis comes on during labor, it is best to terminate labor first and then make sure of the diagnosis and operate on the appendicitis.*

(Alfred Labhardt, 1904)

### 15.8.1 Conservative Treatment

Conservative management in pregnancy is increasing (Fig. 15.20). It ranges from 5.8–9% [34, 195], over 19% [196] to even 67% in population-based studies [194]. In Korea, approximately 25% of pregnancies affected by uncomplicated AA are treated conservatively [197], compared to 63% in China [198].

Three conservative management strategies exist. One is definitive antibiotic treatment [199]. There were attempts to use the transabdominal US to distinguish between uncomplicated and complicated AA as an indicator for definitive antibiotic treatment [199]. Still, there is no consensus on antibiotic therapy route, type, and duration, with reported durations of 3–10 days [42, 200, 201].

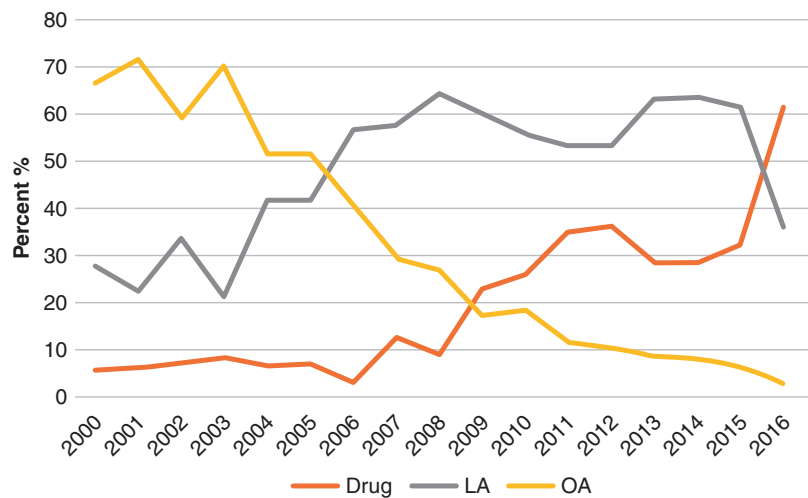
An abdominal MRI is mandatory for the decision on nonoperative treatment [74, 200–204].

Another strategy is to localize the process with interval appendectomy later in the pregnancy or postpartum [74]. During the active disease, US or CT-guided drainage can be performed [205]. Even with image-guided drainage, a lengthy, symptomatic course should be expected [205].

The last option, during active labor, is when delivery is imminent, the operation may be delayed for a short time until the placenta is delivered. Otherwise, immediate appendectomy is advised if prolonged labor is anticipated [40, 69, 206].

Potential advantages mainly related to the fetus include the following:

**Fig. 15.20** Changes in the constituent ratios of the three treatment methods for acute appendicitis in pregnancy. Drug pharmaceutical treatment, LA laparoscopic appendectomy, OA open appendectomy. (Reproduced with permission from [194] under the CC Attribution License)



- Elimination of intra- and postoperative complications,
- Minimization of fetal loss from surgery and anesthesia,
- Elimination of fetal loss from a negative appendectomy,
- Elimination of adverse effects of anesthesia.

Shortcomings of nonoperative therapy include the following:

- 25% failure rate even with uncomplicated AA in first and second trimester [199],
- Increased incidence of recurrent AA during the same pregnancy (see Sect. 15.4.3),
- Unknown impact of antibiotic therapy followed by surgery due to treatment failure on fetal loss,
- Increased incidence of septic shock (6.3×), peritonitis (1.6×), and venous thromboembolism (2×) [34],
- Higher rate of obstetric complications [205].

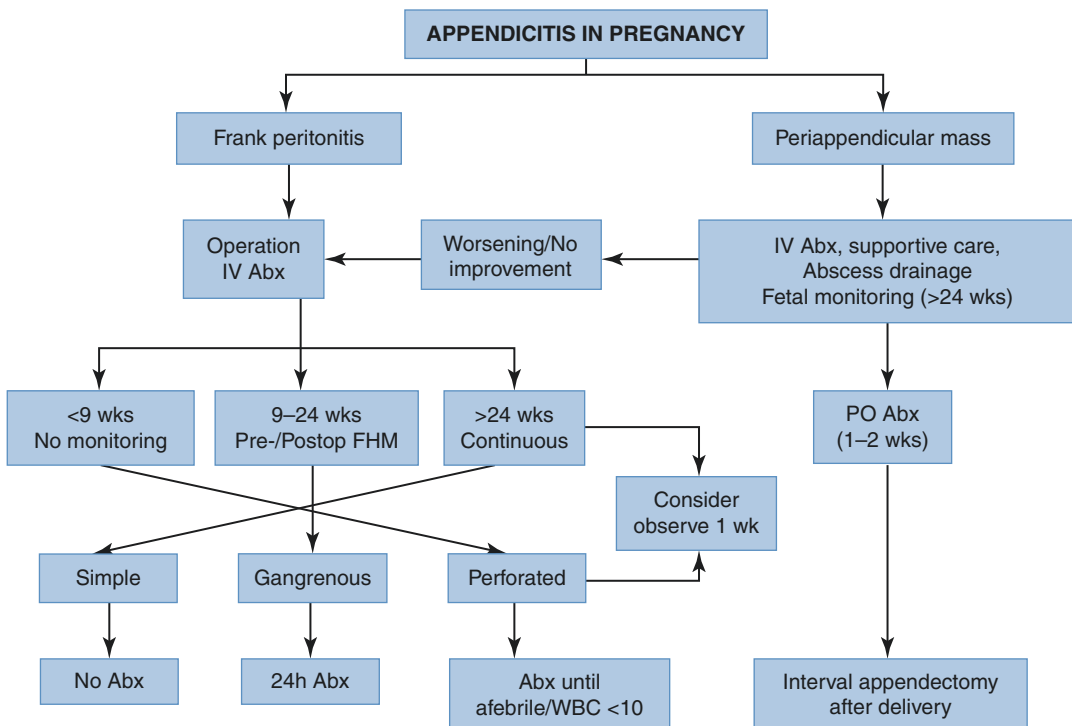
### 15.8.2 Open Appendectomy

*Treat the disease early, regardless of pregnancy.*  
(Paul Fortunatus Mundé)

Until recently, OA in pregnancy predominated, from 60 to 76% [195, 207]. Despite the surgical access, the treatment algorithm is presented in Fig. 15.21.

Several incisions could be used.

- The operation should be completed with (1) minimal or no uterine manipulation, (2) good hemostasis, and (3) prevention of cooling and drying of the uterine surfaces, which increases the risk of postoperative uterine contractions [208, 209]. Temporary exteriorization of the gravid uterus to facilitate operation should be avoided,
- The most experienced abdominal surgeon available should perform the procedure to shorten the operative, anesthesia [210, 211], and immobilization time and reduce potential intra- and postoperative complications.



**Fig. 15.21** Treatment algorithm for acute appendicitis during pregnancy. IV intravenous, PO peroral, Abx antibiotics, wks weeks, FHM fetal heart monitoring, WBC white blood cells

### 15.8.2.1 Muscle Splitting Incision (McBurney's Incision, Gridiron Incision)

This is the incision of choice for the open approach in general and pregnant patients. The advantages are as follows:

- Procedure steps are the same regardless of the gestational age,
- Direct access to the suppurative process without spreading it in clean areas,
- Minimization or elimination of uterine manipulation,
- Extremely low risk of wound disruption or postoperative hernia.

In advanced pregnancy, the incision could be positioned above McBurney's incision and slightly lateral because of possible displacement of the appendix in the RUQ [10]. However, no indication of the change in the location of the incision exists. The appendix is easily located in 94% of the incisions through McBurney's point and in 80% of the incisions above McBurney's point [80, 212].

To prevent compression of the inferior vena cava after 24 weeks of pregnancy, a small rigid pillow under the patient's right buttocks tilts the uterus to the left. It can be used in early pregnancy, as in the general population, to bring closer the ileocecal segment to the anterior abdominal wall.

### 15.8.2.2 Lower Midline Vertical Incision

The incision is preferred with diffuse peritoneal irritation for three main reasons [44] as follows:

- Dealing with unexpected surgical findings,
- Completion of "difficult" appendectomy started through other incisions or laparoscopy,
- Indicated CS performed through the same incision.

When CS is not indicated, there are several disadvantages of midline and paramedian incisions as follows:

- Difficulty of access,
- Much pressure and handling of the uterus to reach the appendix,
- Increased rate of abdominal wall dehiscence in near-term pregnancy due to increased intra-abdominal pressure,
- Increased rate of a postoperative hernia in operations performed in near-term pregnancy due to increased intra-abdominal pressure.

The USA population-based study showed that the laparotomy rate was doubled compared to the nonpregnant population [34].

### 15.8.2.3 Right Transrectal/Pararectal/Paramedian Incision

In 1902 right transrectal incision was favored by Donoghue [213]. He stated that it is easy to reach the appendix. The incision is easy to enlarge without cutting muscle fibers. In healing, the rectus fibers constantly tend to close opening. If the incision is closed correctly, a rupture before, during, or after delivery is minimal.

Currently, these incisions are rarely used. If the diagnosis is certain, then McBurney's incision is made. With diffuse peritoneal irritation, a midline vertical incision is a better option. Before the era of US, when the diagnosis between acute cholecystitis and AA was not clear, the right transrectal incision was also diagnostic. The incision was extended cranially when the appendix appeared normal, and cholecystectomy was performed if indicated. Colin C. McCorriston, in 1963, suggested using the right paramedian incision when the diagnosis was uncertain [214].

## 15.8.3 Laparoscopic Appendectomy

Some recommend routine use of a nasogastric tube due to increased intra-abdominal pressure and pregnancy-related gastric stasis [215].



### 15.8.3.1 Trimester

LA is safe during all trimesters of pregnancy [151, 216–218]. A higher percentage of OA is used during the third trimester [151]. In Columbia, LA is performed in 4.5% of pregnant patients [219].

When LA was introduced in pregnancy, operation times were approximately 50% longer but with decreased length of hospital stay [220, 221]. With the increased use of LA, the duration of OAs and LAs became the same [151]. Currently, the mean operative times are 45 min [222, 223], with longer operating times with advanced gestational age [223]. This is shorter than the median operating time for LA in a nonpregnant population (median 60 min) partly because LA in pregnancy is usually performed by experienced surgeons [223, 224]. No significant difference in the intraoperative complication rates exists between trimesters [223, 225] or OA and LA [224]. Potential disadvantages of LA compared to OA are the necessity of general anesthesia and the inability to perform CS (compared to median laparotomy).

LA has many advantages. Laparoscopy expands the ability to explore the abdomen with less uterine manipulation [226]. Further, it increases the ability to locate and treat dislocated appendix and results in relatively small incisions compared with the OA or helps detect other unexpected causes of acute abdomen [151, 227–229]. Even with the gynecologic disease, neither insertion of additional trocars nor extension of the incision is required [224]. Reduced cecal manipulation during LA with less cecal trauma causes earlier restoration of large bowel function and earlier passage of the first flatus and first postoperative stool. With an open (Hasson) technique for the first trocar placement, the injury to intra-abdominal organs is eliminated. Direct uterine injury during trocar placement has been reported but without a fetal loss [230]. In addition to the general advantage of smaller incisions, less postoperative pain, and earlier return to normal activity, lower rates of abdominal wall dehiscence or herniation during labor are other benefits. Rapid return to full activity could reduce the frequency of maternal thromboembolic events, which are increased in pregnancy [228, 231, 232]. Some found significantly shorter hospital stay in the LA

group [151], while others did not [224, 233]. This can be explained by the LA group being hospitalized for fetal, not maternal surveillance [233]. A Swedish study (1973–1993) evaluated 2233 LA and 2491 OA cases from two million deliveries [234]. Outcomes were evaluated with no statistically significant differences between the LA and OA, and outcomes evaluated birth weight, gestational duration, intrauterine growth retardation, congenital malformations, stillbirths, and neonatal deaths. There was an increased risk for infants in both LA and OA groups to weigh <2500 g, be delivered before 37 weeks and have an increased incidence of growth restriction compared with the total population [234].

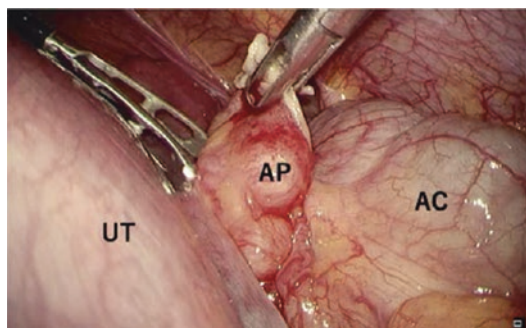
*Laparoscopic appendectomy may be performed safely in pregnant patients with suspicion of appendicitis. Laparoscopic appendectomy can be performed safely in any trimester and is considered by many to be the standard of care for gravid patients with suspected appendicitis. (SAGES clinical practice guideline (2009 and 2011))*

### 15.8.3.2 Pneumoperitoneum

See Chap. 3.

### 15.8.3.3 Laparoscopic Technique

In the first and early second trimesters, trocar position and technique are similar to nonpregnant patients. The third trimester poses difficulty because of (1) the diminished working space from the enlarging uterus (Fig. 15.22), (2) the risk of injuring the uterus, and (3) the risk of excessive manipulation of the gravid uterus leading to preterm labor. In advanced pregnancy, the port positions are slightly different (see further text). The patient is placed supine on the operating room table. Restraining straps are placed across the chest and thighs, and sequential pneumatic compression devices are placed on both lower extremities. Some recommend a Foley catheter [236] and a nasogastric tube placement with removal at the end of the operation. Maternal end-tidal CO<sub>2</sub> is monitored and kept within the physiological range (30–40 mmHg).



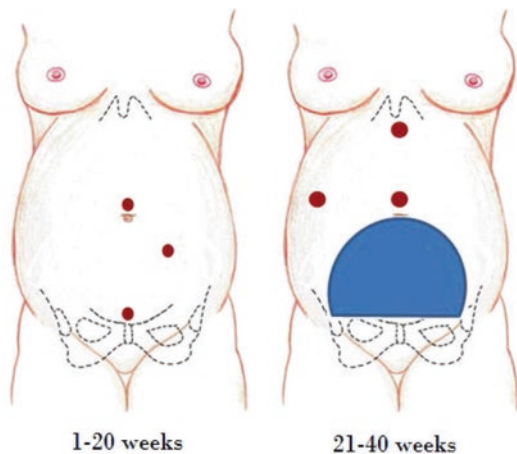
**Fig. 15.22** Laparoscopic appendectomy at 32 weeks of gestation. The appendix (AP) was extracted between the uterus (UT) and the ascending colon (AC). (Reproduced with permission from [235])

Patients are tilted to the left to displace the uterus from the inferior vena cava with the removal of the small bowel from the operating field and a slight Trendelenburg position, if necessary. The procedure is performed using three ports, and their placement is modified by gestational age. In advanced pregnancy, the first port for a laparoscope (5 or 10 mm) is placed 2–4 cm cephalad to the gravid uterus in the upper mid-line between the umbilicus and xiphoid process. The bigger the uterus, the more cranial the first trocar is placed for easier intraperitoneal manipulation.

Modifications of trocar sites and size depend on the laparoscopic technique and equipment. Some recommend placing the second port (5 or 12 mm) laterally in the RLQ and the third port (5 or 10 mm) in the RUQ in a more cranial location. When the linear cutting stapler is used for the transection of the appendix at its base 12 mm port is necessary [237]. Other combinations of trocar placement are presented in Fig. 15.23, depending on the degree of uterine enlargement [236].

The evacuation of infected liquid in the recto-uterine pouch could be inadequate in the second half of pregnancy. It is difficult to reach the pouch without uterine manipulation. It is essential to eliminate infective fluid to avoid pelvic abscess formation and eliminate the possibility of uterine irritability with its consequences (see Chap. 4).

*Single-port laparoscopy* is used in small series. The method is feasible but without conversion to OA, but (1) 33% rate of conversion to



**Fig. 15.23** Different trocar positions for a laparoscopic appendectomy in different stages of pregnancy

reduced-port laparoscopic appendectomy and (2) an increased rate of wound complications (8%) [238] and additional port [238].

## 15.8.4 Perioperative Considerations

See Chap. 2.

### 15.8.4.1 Pathohistological Examination

Extracted specimens should be sent for pathohistological examination because, especially in the pregnant patient group, other pathologies were common [151] before the era of MRI.

Pregnancy complicated with appendiceal endometriosis (AE) ranges from 3–8/10,000 deliveries [239], with less than 30 cases of AE mimicking AA in pregnancy being published. Hematoxylin-eosin shows AA, and the appendiceal wall has foci of endometrial implants with acute inflammation. A panel of immunohistochemical stains, including cytokeratins CK7 and CK20, estrogen receptor, and CD10, PAX8, can differentiate intramural glands and appendiceal mucosa, as the former react as endometrial mucosa. In contrast, the latter responds as a colonic-type mucosa [240]. Cytoplasm positivity of valentine, the nuclear presence of progesterone receptors, and the lack of pan-cytokeratin,

HMB-45, and calretinin are characteristic of decidualosis. A decidual polyp, which occludes most of the appendiceal lumen, is an extremely rare cause of AA during pregnancy.

#### 15.8.4.2 Postoperative Course

LA's potential advantages in pregnant patients include decreased fetal depression due to lessened postoperative narcotic requirements, lower risks of wound complications, and diminished postoperative maternal hypoventilation (see Chap. 21). A nasogastric tube is extracted after the operation, and early ambulation starts after several hours. Without postoperative nausea and vomiting, oral fluids could be commenced within 12 h after the operation.

## 15.9 Specific Considerations

### 15.9.1 Normal Appendix

#### 15.9.1.1 Incidence

NARs during pregnancy and through decades (1951–1954 up to 65%; up to 1973 up to 42%) vary considerably (4–65%) [10, 13, 14, 19–26, 28, 29, 37, 68, 88, 153, 168, 175, 176, 216, 236, 241–245]. Before the CT era, NAR in the general population ranged from 10 to 15% and as high as 26% among reproductive age females. The difficulty in making a clinical and radiological diagnosis particularly close to term, combined with the high incidences of fetal mortality and maternal morbidity from appendiceal perforation, has led to a low threshold for surgical intervention.

The combination of physical examination, US, and CT has the lowest NAR [168]. NAR with clinical evaluation only is 54%, 36% in the clinical assessment and US group, and 8% in the US and CT scan group [168]. Recent studies without abdominal CT use have a lower incidence of NAR (11% and 16%, respectively) [80, 232]. With the increased use of abdominal CT, the NAR declines without the cost of a higher perforation rate but with the additional risk of radiation consequences.

The highest NAR is during the second trimester [47]. However, some claim similar NAR in the second and third trimesters (18% in the first, 40% in the second and 3rd [26, 246]), partly because obstetric complications from abdominal operations are the rarest in the second trimester. There is a decreased risk of NAR in the puerperium. Puerperal women are less prone to seek care for abdominal pain [47] and more liberal abdominal CT use in the puerperium.

NA does not mean negative exploration. Approximately 15–20% of patients with a normal appendix have another pathology (e.g., ovarian cyst, ovarian torsion, mesenteric adenitis, fibroids, and salpingitis) [176]. No significant difference in NAR between LA and OA exists [236].

The fetal loss rate of 2–3% for both NA and non-perforated AA is reported [208, 247]. Its relation to the type of procedure, undetected underlying pathology, or fetal loss rate in general pregnant patients is unclear.

#### 15.9.1.2 Appendectomy

Removing the “normal” appendix to rule out AA histologically and eliminating AA's differential diagnosis with recurrent symptoms is recommended. The gross changes are not visible if intramural or mucosal changes in the appendix exist responsible for the symptoms. Approximately 9% have recurrent RLQ pain after negative laparoscopy without appendectomy [248], and 20–22% who underwent appendectomy responded very well to appendectomy despite a normal microscopic examination of the appendix. The explanation is functional appendiceal conditions such as appendix colic, appendicopathy, or appendiceal fecalith without acute inflammation [249, 250]. Up to 30% of intraoperative diagnoses of normal appendix confirmed inflammation histologically [251]. These conclusions are similar to SAGES guidelines for LA in the general population (04/2009): *If no other pathology is identified, the decision to remove the appendix should be considered but based on the individual clinical scenario. Macroscopically normal appendices may have abnormal histopathology. Several studies have shown a 19–40%*

*rate of pathologically abnormal appendix in the setting of no visual abnormalities. Therefore, the risk of leaving a potentially abnormal appendix must be weighed against the risk of appendectomy in each scenario.*

Furthermore, appendiceal inflammation/obstruction can be due to appendiceal neoplasms. If pseudomyxoma peritonei is found, the appendix should be removed and sent for a histological examination.

*As a surgeon, you should not be deterred from removing an appendix once the diagnosis is suspected because pregnancy is not affected by removing a normal appendix [252].*

### 15.9.2 Incidental Meckel's Diverticulum

Given the high incidence of perforation (57%) resulting in significant maternal and fetal mortality, removal of incidentally found MD is justified [124], especially when: (1) future pregnancies are desired and (2) specific diagnostic difficulties during pregnancy are expected.

The benefits of removing an incidental MD in the general population are far superior to the risk of developing complications. If any of the following criteria are fulfilled, the incidental MD should be removed [253]:

- Patient age <50 years,
- Male sex,
- MD length >2 cm,
- Ectopic or abnormal features within a diverticulum.

When one, two, three, or all four criteria are met, the proportion of symptomatic MD is 17%, 25%, 42%, and 70%, respectively [253].

Laparoscopic treatment is rare partly due to simultaneous CS in advanced pregnancy [122]. If the asymptomatic MD or symptomatic MD is found, *diverticulectomy* or *wedge small bowel resection* with subsequent bowel continuity is performed during OA and LA. During LA, an endoscopic linear cutting stapler is introduced through a 12 mm trocar and applied to the base of the MD, perpendicular to the base of the MD, but transverse to the longitudinal axis of the bowel. The stapler is fired, and the MD resected off the ileum. Small bleeding points at the edge of the staple line are sutured intracorporeally with 3–0 resorbable sutures. The specimens are delivered through a 12 mm port (which can be extended if needed) using a bag if needed. A wedge resection is rarely necessary for incidental MD because the base is not inflamed. If suture techniques are used after excision, bowel continuity is achieved by placing intracorporeal sutures with 2–0 or 3–0 resorbable sutures. Specimens should always be sent for pathohistological examination. The hospital stay is 7.9 days for open surgery and 4.6 days for laparoscopic surgery [122].

Since 1990 symptomatic and removed MD does not increase maternal mortality, which is 0%. An increased rate of premature labor is observed, with fetal mortality of 7.4% [122].

Delayed surgical treatment of symptomatic MD increases fetal mortality [122].

### 15.9.3 Ectopic/Heterotopic Pregnancy

#### 15.9.3.1 Incidence and Pathophysiology

Ectopic pregnancies (EP) occur in approximately 16/1000 patients [254], with the rarest form of heterotopic pregnancy (HP). Around 30 cases of EP/HP have been reported in conjunction with

AA since 1960 [254–269]. EP may trigger AA through a contiguous initial inflammation, creating a portal for infection in the appendix by normal colonic bacterial flora, so-called *periappendicitis* [255]. Lymphoid hyperplasia causes luminal obstruction. A subsequent increase in intraluminal pressure results in ischemia of the appendiceal wall. This could be a reason for the development of AA up to 1 week after (the treatment) of EP [254, 261]. In the opposite direction, an antecedent AA with spontaneous resolution could also conceivably result in peritubular inflammatory adhesions favoring the development of the EP. It is of particular interest that 75% of tubal pregnancies involve the right tube [23]. Also, concurrent EP and AA show right-sided tubal EP predilection (75%) versus left tubal EP (16%) [255]. HP with AA is challenging due to potentially three causes of abdominal pain as follows: appendix, intrauterine, and extrauterine pregnancy [262–264].

### 15.9.3.2 Clinical Presentation

Hickam's dictum, after the late Dr. Hickam from Duke University, is the following quotation "*Patients can have as many diseases as they damn well please.*" Thus, with mixed clinical presentation, both pathologies could be present (see Chap. 9). Even a concurrent appendiceal EP, carcinoid tumor, and AA case were published [270].

### 15.9.3.3 Diagnosis

Although advances in transabdominal and transvaginal US and highly sensitive  $\beta$ HCG tests have facilitated the earlier diagnosis of EP even before the onset of clinical symptoms, differences in operator technique and obscuring bowel and gas may render a diagnosis of AA or EP inconclusive [266]. The discriminatory zone is the level of  $\beta$ HCG at which findings of a normal IUP are expected to be visualized on US. It is often considered 1500 and 6000 mIU/mL for transvaginal and transabdominal US, respectively [271], although  $\beta$ HCG levels cannot reliably discriminate between early intrauterine pregnancy and EP [271]. With high clinical suspicion, the inconclusive US should not preclude a AA and EP/HP

[29, 46, 255, 262]. Another option is to use abdominal MRI with excellent sensitivity and specificity for AA (see Sect. 15.7.5) and EP (see Chap. 9).

### 15.9.3.4 Treatment

An uncertain diagnosis indicates emergent exploration by (mini)laparoscopy or laparotomy [255, 259, 260] when the hemorrhagic shock is encountered. Appendectomy is recommended if Fallopian tube sparing surgery is performed due to the following: (1) no additional postoperative morbidity and risk of postoperative complications, (2) further pregnancies or recurrent EPs have a shorter list of differential diagnoses in patients with lower abdominal pain, (3) elimination of future AA in this high-risk group (younger age and right-sided recurrent EP) [254], and (4) future AA can cause periadnexal adhesions increasing the risk of recurrent right-sided EP.

If the appendix appears normal, Meckel diverticulitis should be ruled out. With AA with amenorrhea in early pregnancy or a small amount of blood in the pelvis, ectopic pregnancy should be ruled out.

## 15.9.4 Assisted Reproductive Techniques

### 15.9.4.1 Incidence

EP/HP occurs in 1–3% [272, 273] of IVF-ET pregnancies, while HP has been estimated at 1/30,000 non-IVF pregnancies [272]. The transfer of four or more embryos poses an additional risk for HP [273]. Five AA cases in IVF-ET pregnancy pose significant incidence compared to non-IVF pregnancies (24 cases—see Sect. 15.9.3.1). Of these, two cases had HP (9 weeks [260] and 6 weeks [264]). The remaining two are iatrogenic appendiceal punctuations with the needle for oocyte retrieval and subsequent development of perforated AA [274, 275].



#### 15.9.4.2 Differential Diagnosis

With IVF-ET pregnancies, AA and EP should be included in the differential diagnosis [264].

#### 15.9.4.3 Diagnosis

Indicative of iatrogenic appendiceal injury is the development of AA up to 9 days following the IVF procedure [274, 275].

#### 15.9.4.4 Treatment

Both patients underwent right salpingectomy and appendectomy and delivered by CS. The third case described a woman with a perforated appendix and an EP [259]. During a (diagnostic) laparoscopy, the appendix and adnexa should always be examined in IVF patients despite normal intrauterine pregnancy, especially if AA is proven intraoperatively with fresh blood in the pelvis or around the adnexa or appendix. This rule confirms that  $\beta$ HCG in HP is elevated due to normal intrauterine pregnancy and is not diagnostic for HP.

Appendectomy is mandatory (Fig. 15.24), while management of simultaneous ruptured EP/HP includes the following:

##### *Ruptured HP*

1. Intrauterine pregnancy preserved,
2. Salpingectomy or salpingotomy.

##### *Ruptured EP*

1. Salpingectomy or salpingotomy.

The benefits of salpingectomy over salpingotomy are uncertain. Salpingectomy is easier and safer, especially with a live intrauterine pregnancy. It reduces the risk of complications such as persistent bleeding or retention of trophoblastic tissue after salpingotomy [272]. Salpingectomy is recommended if fallopian tubes are significantly damaged and not functional for further spontaneous pregnancies. Salpingectomy could be considered with a healthy contralateral fallopian tube, as this treatment does not preclude future fertility. For unruptured EP/HP, therapeutic recommendations are as follows:

##### *Unruptured HP*

1. Intrauterine pregnancy preserved,
2. Salpingectomy or salpingotomy.

##### *Unruptured EP*

1. Methotrexate.

Even simultaneous ovarian hyperstimulation syndrome (OHSS) with AA is described [276]. Epigastric pain is not an uncommon symptom in patients with severe OHSS with massive ascites. Pyrexia is common with severe OHSS without infection [277]. A WBC count is elevated with severe OHSS [278] and AA. The possibility is raised that OHSS might affect the course of concurrent AA. An increased rate of infectious diseases was reported with OHSS, possibly due to immunodeficiency from hypoglobulinemia, frequent with severe OHSS [277]. Severe stress associated with symptoms of OHSS, a hospital stay, multiple monitoring, and therapies might also impair immunoprotective status. It may be that AA with OHSS could be more aggressive and is more likely to rupture than without OHSS. Once bacteria are seeded into the peritoneal cavity asso-



**Fig. 15.24** Laparoscopic view of unruptured ectopic pregnancy of the right fallopian tube. The knot is placed on the base of the antecedent appendectomy (arrow). (Reproduced with permission from [267])

ciated with OHSS, they may grow rapidly to form abdominal abscesses because the ascitic fluid of OHSS serves as an excellent culture medium for bacteria with its rich source of nutrients, including albumin [279]. OHSS, complicated by intraperitoneal inflammatory disease, may worsen its potentially life-threatening condition.

For patients with the risk of severe OHSS, such as rapidly increasing estradiol levels or massive follicular recruitment, a decrease in medication dosages or alteration of the ratio of individual medications in the regimen could be attempted. However, these medications should be withdrawn if the non-obstetric acute abdomen is suspected or proven. In the single case of OHSS with perforated AA, there is no mention of complications during the prolonged (37 days) postoperative course or perioperative care except for appendectomy and antibiotics [276].

### 15.9.5 Prognosis

Low birth weight and macrosomia are associated with immediate and long-term risks to offspring, including IVF singletons [280, 281]. The factors leading to infertility may be responsible for the adverse perinatal outcome rather than the process itself [282]. Maternal characteristics—maternal age, the source of the oocyte, and cervical causes of infertility—are strongly associated with the risk of low birth weight and preterm delivery in singleton live births resulting from IVF. Notably, some associations were opposite to those seen for successful live birth. Thus, in women who successfully have an IVF singleton live birth, the risk of low birth weight is reduced in older compared to younger women. Low birth weight and preterm birth are reduced when the woman's embryo has been used [283].

### 15.9.6 Sickle Cell Disease

#### 15.9.6.1 Incidence

The incidence of AA depends on the prevalence of SCD in different world regions. In Saudi Arabia, the incidence is 16.9% [284]. The inci-

dence of AA is lower in a nonpregnant population with SCD than in the general nonpregnant population [283, 285]. Also, homozygous SCD is now widespread and has broad clinical variability.

#### 15.9.6.2 Clinical Presentation and Laboratory Findings

Around 75% of the SCD patients reported pain in their RLQ [286], the same percentage as in pregnant nonsickler patients [29]. Vomiting is common (67%) [286] and is comparable to pregnant nonsickler patients with AA [287]. Only 50% of the AA patients had a fever, while none of the sickler patients had pyrexia in the normal appendix group. Around 75% of the AA patients with SCD had WBC  $>16,000/\text{mm}^3$  [286]. There is a significant difference in the WBC counts in AA patients compared to those with non-inflamed appendices [27]. As with nonsickler patients, delaying the appendectomy beyond 24 h in their third trimester is associated with gangrene and appendiceal perforation [20, 286, 288].

#### 15.9.6.3 Prognosis

Pregnancy in SCD patients presents a clinical challenge as maternal mortality is 1–2% and perinatal mortality is 5–6% [289, 290]. Maternal mortality is rare in pregnant nonsickler patients with AA (see Sect. 15.10.3.1), similar to SCD patients [286]. The fetal loss and premature delivery rates were 9 and 18%, respectively, consistent with other reports [15, 21]. The variability of complications [291] may be due to the milder form of SCD in the Al-Hassa area (high levels of HbF). The high HbF levels protect against several clinical features associated with SCD, but the association between HbF levels and the severity of the disease process is complex [289].

### 15.9.7 Appendiceal Endometriosis/Deciduosis

#### 15.9.7.1 Historical Considerations

During pregnancy, the ectopic decidua (deciduosis) is attributed to hormonal effects on the ectopic endometrium, namely endometriosis, or normal subceolomic mesothelium. Karl von

Rokitansky first described AE in 1860 [292]. Hirschberg, in 1905, coined the term *periappendicitis decidualis*, describing a patient with AE with right-sided tubal EP [293]. Sampson proposed the theory of retrograde menstruation as the etiology for endometriosis [294] and reported AE. Bogatko described the first AA due to AE in 20 weeks of pregnancy in 1949 with the uneventful postoperative course and later CS [295].

#### 15.9.7.2 Incidence

Deciduosis is a benign condition not correlated with obstetrical complications during pregnancy. This physiological phenomenon is present in 10% of the CS on the ovary, uterine, and fallopian tube serosa and is associated with abdominal pain during pregnancy [296]. Ectopic decidual glands is subclassified as decidualized endometriosis, whereas, without glands, the condition is called deciduosis.

AE is rare in the general population, occurring in 0.2–0.3% of appendectomy specimens [297]. AE accounts for 0.0075–0.045% of extrapelvic endometriosis [298] and 1% of pelvic endometriosis [299] in the general population. The prevalence of AE in patients with biopsy-proven endometriosis or chronic RLQ pain is 4.1 and 3.7%, respectively [300, 301]. Pregnancy complicated with AE is rare, ranging from 3–8/10,000 deliveries [239]. There are less than 30 cases published during pregnancy. Compared to AA, the occurrence is higher during the third trimester.

#### 15.9.7.3 Risk Factors

No differences were found when age, parity, and pregnancy duration at diagnosis were compared for women experiencing AE and AA during pregnancy [26, 47, 302]. With pelvic endometriosis, the odds ratio for AE was 20.9 compared to the general population [300].

#### 15.9.7.4 Clinical Presentation

Isolated AE in the general population is usually asymptomatic. The lesions are discovered incidentally in appendectomy specimens or colonoscopies with an inverted or bulbous appendiceal orifice. Cyclic RLQ pain during menstruation is

typical before pregnancy. In pregnancy, the frequency of the presenting symptoms and signs, such as abdominal pain, nausea, vomiting, and elevated body temperature, does not differ between acute AE and AA. Therefore, the presentation does not help establish the diagnosis [239, 240, 294, 301, 303–320]. In contrast to AA, the incidence of AE is much higher during the third trimester [302].

#### 15.9.7.5 Diagnosis

WBC counts are similar in acute AE and AA and do not help establish the preoperative diagnosis [239, 240, 294, 301, 304–321]. Leukocytosis due to deciduosis (or normal pregnancy) is from the production of granulocyte colony-stimulating factor [322]. The gold standard to diagnose EA is exploration, done in a standard fashion for AA (see Sects. 15.8.2 and 15.8.3).

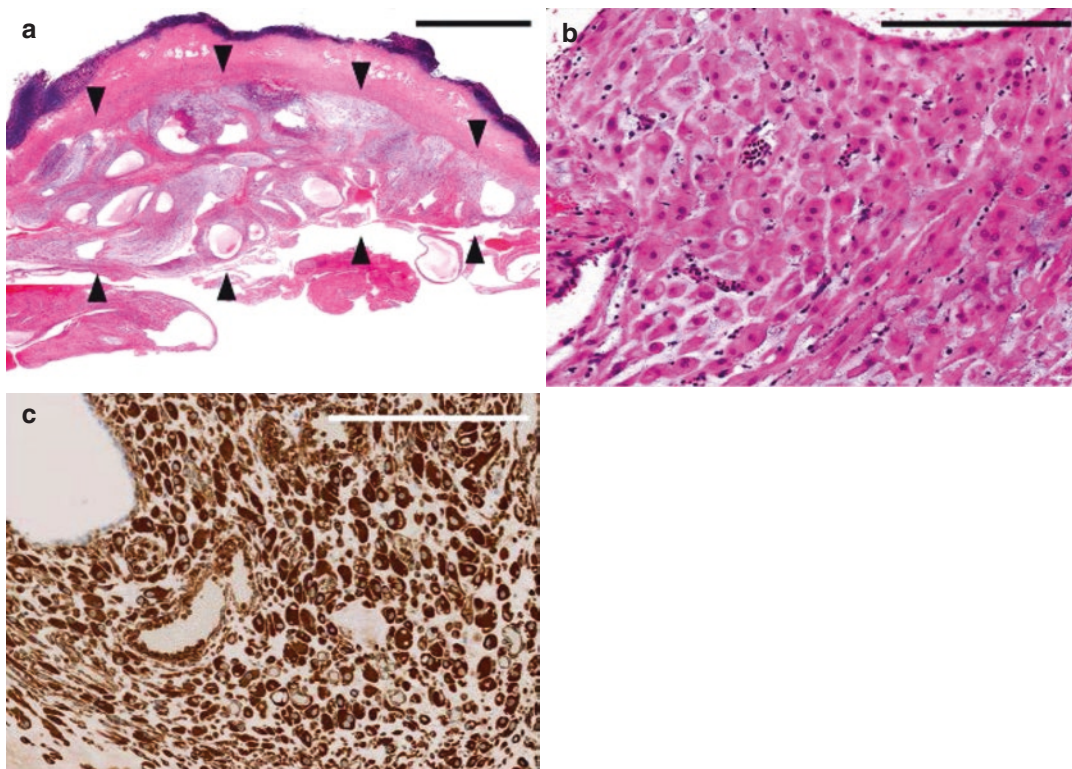
Histopathology gives a definitive diagnosis (Fig. 15.25).

#### 15.9.7.6 Prognosis

The overall AE complication rate is higher than with AA, especially during the third trimester, partly because the incidence is the highest during the third trimester. Intra-appendiceal decidual cells induce a higher inflammatory response resulting in a higher occurrence of transmural lesions, which increase the risk of perforation [314]. Approximately 27% of cases during pregnancy were perforated, all cases during the third trimester. There were no maternal or fetal complications in 45% of the cases [302].

### 15.9.8 Appendiceal Carcinoid

Even in the general population, tumors of the appendix are rare. The most common is appendiceal carcinoid which accounts for 85% of appendiceal tumors [324], with a median age of 29.8 years [325]. In 80%, the appendiceal carcinoids are incidentally discovered in the removed organ without signs before surgery. Carcinoid tumors are found in the general population in 0.3–0.9% of appendectomy specimens [326]. Several cases of appendiceal carcinoid in preg-



**Fig. 15.25** (a) Area of deciduositis, accompanied by myxoid degeneration, in the subserosal layer (area marked by arrowheads) of the tip side (bar: 2.5 mm). (b) In a high-power magnification, deciduositis comprises large polygonal cells with abundant eosinophilic cytoplasm and

centrally placed uniform nuclei, characteristic of decidual cells (bar: 2.5  $\mu$ m). (c) Immunohistochemical evaluation shows diffuse positivity for vimentin in the decidual cell cytoplasm (bar: 250  $\mu$ m). (Reproduced with permission from [323] under the CC Attribution License)

nancy presented as AA [327–332]. Berriors et al. published the first case in 1965 [331]. The interaction between the carcinoid tumor of the appendix and pregnancy has not yet been elucidated [329].

Postappendectomy management during pregnancy depends on (1) tumor diameter (2 cm), (2) tumor localization, (3) tumor grade and stage, and (4) weeks of gestation.

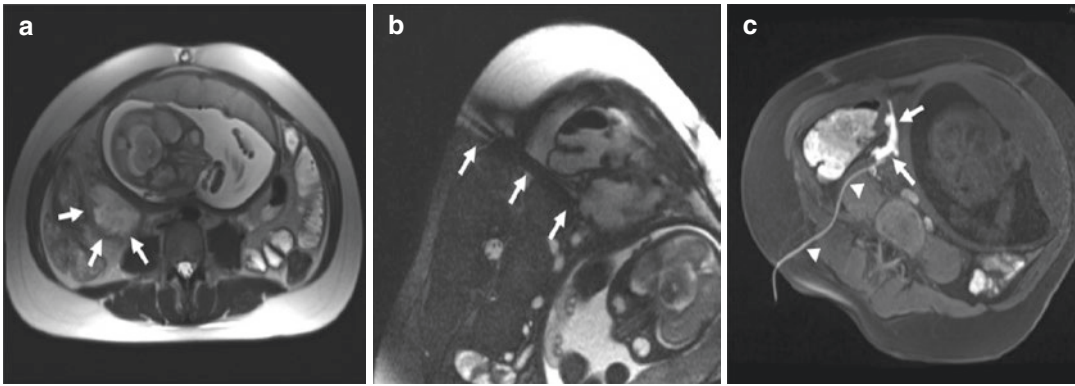
The right hemicolectomy is indicated several weeks after delivery if the tumor is on the appendiceal base or is >2 cm [329]. If CS should be performed due to obstetric indications, a right hemicolectomy should be performed after CS during the same operation.

*Medical treatment like somatostatin analogues and avoiding conditions and substances that cause flushing may be useful during pregnancy.* (North American Neuroendocrine Tumor Society [333])

### 15.9.9 Perityphlitic/ Postappendectomy Abscess

The appendiceal abscess should be drained without delay due to the high risk of rupture, especially in pregnancy. The growing uterus during pregnancy, the contracting uterus during labor, and the shrinking during puerperium form the





**Fig. 15.26** (a) T2-weighted MRI shows hyperintense abscess formation (arrows) posterior to the uterus. (b) After positioning in the left lateral decubitus position, a nonferromagnetic needle (arrows) is placed in the lesion using balanced steady-state free precession sequences. (c)

After catheter placement, diluted gadobutrol was instilled in the abscess (arrows) via the drainage catheter (arrow-heads) to evaluate the completeness of drainage. (Reproduced with permission from [334])

unstable inner boundary of the abscess, increasing the possibility of rupture [48]. The highest risk of rupture occurs during labor when the uterus contracts, later shrink, and has a significant impact on disseminating pus with the possibility of contamination of the genital tract. An abscess can be drained by radiology interventional techniques. The patient is in the left lateral decubitus position. MRI-guided puncture through the right psoas muscle is the only safe access to the lesion without other interposing structures. (Fig. 15.26). After a successful puncture, pus is aspirated and sent to microbiology. The resolution of an abscess can be re-evaluated with MRI [334].

lize the minimal intra-abdominal pressure necessary for adequate exposure. Although evidence suggests a fascial separation occurs early, it remains to be seen what long-term status these incisions will achieve. No hernia has developed in these patients with a follow-up of 5.5 years [335].

## 15.10 Prognosis

*The mortality of appendicitis complicating pregnancy and the puerperium is the mortality of delay.*  
(Edmund Adam Babler, 1908)

### 15.9.10 Puerperium

The unique consideration in the postpartum patient is the presence of a healing abdominal incision after CS. There are no studies on outcomes for recent abdominal incisions subjected to early pneumoperitoneum. Commonly, pneumoperitoneum is limited to 10 mmHg in CS patients. This prevents undue mechanical strain on the healing wound, though there were no controls for comparison with the standard pressures (15–16 mmHg). It seems prudent to uti-

#### 15.10.1 Conservative Treatment

Previous studies of conservative treatment found a significant increase in maternal morbidity—septic shock (6.3×), peritonitis (1.6×), venous thromboembolism (2×) [34], and perinatal adverse events—preterm labor and spontaneous abortion [195]. This was not confirmed in the largest population-based study [194]. The higher maternal mortality rate was found in nonoperated pregnant patients [336], although a recent study was without maternal mortality [42]. There was no significant difference in ges-



tational age at delivery, mode of delivery, birth weight, and APGAR scores between conservatively and operatively treated groups [42]. The most recent population-based study did not find a higher fetal loss rate (5%). The authors claim no recurrence of AA before fetal losses. They concluded that the fetal loss might have occurred due to other causes [194]. Gestational age and maternal age are two major risk factors for fetal loss. Therefore, these two factors should be included when comparing treatment outcomes for fetal loss. Potentially, the bias results from lower degrees of appendiceal inflammation treated nonoperatively and included patients without AA.

### 15.10.2 Perforation Rate

Previously, the perforation rate in pregnancy has been reported as high as 55–60% compared to 4–19% in the general population [38, 45, 208, 220, 337]. Up to 1908, the perforation rate was 64% [338]. When the operation is delayed >24 h, a perforation rate is 66% compared to 0% with the operation <24 h after the presentation [45]. The timing of intervention varies by trimester: 90% in the first trimester undergo the operation within 24 h of the onset of symptoms. In the third trimester, up to 64% have symptoms >48 h before operation [109, 339]. Diagnostic and therapeutic delay >48 h is more common during labor and the early puerperium [50, 340–342]. Perforation increases the risk of generalized peritonitis because the omentum cannot isolate the infection [46]. Diagnostic and therapeutic delay is more common during the early puerperium due to the following:

- Painful and prolonged labor masks symptoms of AA,
- Epidural analgesia during labor suppresses symptoms of AA,
- Abdominal pain affects up to 98% of postpartum women [343, 344],
- Leukocytosis and fever are especially exaggerated in the early puerperium.

The trend in the perforation rate is decreasing from 25–29% [80, 345] to 15–20% during the last several decades [24, 34]. The perforation rate through the trimesters increases: 6–8.7%, 10–12.5%, and 13–26.1%, respectively [24, 47]. In summary, the causes for the treatment delay include [50, 109, 229, 339, 340] the following:

- *Atypical clinical picture* when observation delays the intervention,
- *Time delay during consultations* if departments/institutions are dislocated,
- *Time delay during the patient transfer* if departments/institutions are dislocated,
- Third trimester, *painful labor* and early puerperium,
- *Epidural analgesia* during labor suppresses the symptoms of AA,
- *Lower CT use* during pregnancy.

### 15.10.3 Maternal Outcome

#### 15.10.3.1 Maternal Mortality

Before 1900, maternal mortality was 30%; with perforation operated even without delay, it was up to 58% [56, 346], while up to 100% when diffuse peritonitis was present [337, 347]. Up to 1908, maternal mortality was 24%, but 45% with diffuse peritonitis [348]. Since 1950, mortality has decreased partly due to the introduction of antibiotics. In 1947, maternal mortality was lowered to 0.71% when the disease was confined to the appendix, 30% with peritonitis, and 50% when perforated [349]. In 1954, cases occurring in the last 3 months of pregnancy showed a mortality of 20.7% [350]. Until 1992, appendiceal perforation had maternal mortality up to 4% compared to <1% in non-perforated AA [345]. Today, overall, maternal mortality is <1% [27–29, 46], or even 0% even with perforated AA [80, 244, 351]. It is rare in the first trimester and increases with advancing gestational age due to the prolonged period between admission and operation in the third trimester [46, 109, 252]. For comparison, with MD during pregnancy

(patients since 1949 included), maternal mortality was 17% [124]. In all deceased patients, MD perforation was present [124]. The likelihood of maternal death in the USA is higher in the non-Hispanic black population compared to the non-Hispanic white population and Hispanics (OR: 4.42 vs. 4.04 vs. 3.62, respectively) [39]. This could be explained by underlying preexisting conditions such as uncontrolled diabetes, hypertension, and cardiac conditions.

Adverse maternal (and fetal outcomes) are associated with [21, 39, 45, 151] the following:

- A delay in surgery (>24 h after onset of symptoms),
- Appendiceal perforation,
- Maternal temperature >38 °C,
- Leukocytosis >16,000/mm<sup>3</sup>,
- Non-Hispanic black population (USA).

### 15.10.3.2 Maternal Morbidity

Increased maternal morbidity associated with AA was partly due to the increased peritonitis rate [207]. Maternal morbidity with LA is the same [195] or less [233] compared to OA. The advantages of laparoscopy include (1) decreased surgical trauma with lesser use of analgesics, especially opioids that can lead to fetal depression, (2) decreased gravid uterine manipulation, (3) minimal use of electrosurgery in the proximity of the uterus, (4) earlier recovery of bowel function with shorter time to oral intake and therefore less nutritional stress to the fetus, (5) early mobilization with a lesser risk of thromboembolic risk associated with pregnancy, (6) shorter postoperative length of stay in the hospital, and (7) faster return to daily activities [151, 195, 225, 227, 236, 352–354]. Sometimes, a similar hospital length of stay after OA and LA is because the LA group is hospitalized for fetal surveillance, not maternal postoperative surveillance [233]. LA in pregnancy is safe and effective, without any long-term effects on the mother [355].

CS rates are similar in pregnant populations with and without AA, consistent with teaching promoting CS only for obstetric indications [207]. The degree of appendiceal inflammation

does not influence the type of *delivery at term*, with half of the patients having CS and another half having vaginal delivery in both non-perforated and perforated groups [93]. However, the rate of CS is almost doubled in the presence of peritonitis. This likely reflects the increased severity of maternal illness and possible fetal compromise requiring (1) an appendectomy with simultaneous delivery or preterm delivery early after appendectomy [74, 207]. Approximately 12% underwent CS as the mode of delivery and 7% at the time of appendectomy [24].

## 15.10.4 Fetal Outcome

### 15.10.4.1 General Considerations

The effects of any medical intervention on fetal mortality must be considered in the context of certain preexisting background risks common to all pregnancies. These include a 3% risk of birth defects, 15% for miscarriage, 4% for prematurity, 4% for growth retardation, and 1% for mental retardation or neurological developmental problems. A variety of non-obstetric surgical interventions resulted in a spontaneous miscarriage (5.8%), premature delivery (8.2%), and major birth defects (2%) [102].

Surgery (appendectomy) and general anesthesia are not significant risk factors for spontaneous abortion and do not increase the risk of major birth defects, even during the first trimester.

### 15.10.4.2 Historical Perspective

In the nineteenth century, many pregnant patients with AA presented with the consequences of advanced intraperitoneal inflammation. In that period, miscarriage and preterm labor resulted in fetal mortality of 100% [103, 104, 356]. Fetal mortality was higher in the years before 1990 when the current possibilities offered by modern neonatology, fast and accurate (imaging) diagnostic workup, intensive care, and antibiotic therapy were limited or not available. Abrahams, in 1897, collected 15 cases

from the literature and stated that the fetal mortality in cases of perforative AA during pregnancy, even when operated upon without delay, was up to 90% [56]. Until 1908, fetal mortality was 40%. Edmund Adam Babler concluded that “the mortality of appendicitis complicating pregnancy is the mortality of delay” [348]. This statement was published several years earlier by Heaton [53]. Until 1973, fetal mortality was 20% (perforated AA 30% and non-perforated AA 3%) and seemed to be related to the severity of the disease rather than the period of gestation [244].

#### 15.10.4.3 Fetal Mortality

Without appendiceal perforation, fetal mortality is 0–5% [22, 24, 40, 69, 80, 93, 351], while perforation raises fetal mortality to 10–36% [24, 27, 28, 69, 80, 93, 351]. For a comparison, fetal mortality of 13.6% (1949–2005) was found when MD in pregnancy was the cause of acute abdomen [124].

Apart from premature labor, the risk of intrauterine fetal death increases if the infant remains in utero in the presence of peritonitis. One reason is the rare incidence of infection-induced placental abruption (see Sect. 4.7.2). Another is high pyrexia and bacterial toxemia (see Chap. 4). The adjusted odds for fetal loss increased significantly for the non-Hispanic black population with AA in the USA. They were about three times as likely to experience fetal death as the non-Hispanic black population without the disease [39].

#### 15.10.4.4 Fetal Morbidity

Approximately 17% of women with AA deliver in the same admission, with a 3× increase in preterm birth [207]. Unexplained antepartum hemorrhage was 4×, and placental abruption was 2× more likely with AA. The systemic inflammation associated with AA and the proximity of the appendix to the uterus may lead to transuterine neutrophil and inflammatory cytokine infiltration (chorion and amnion) and lead to placental abruption or preterm birth [207]. Premature rupture of membranes and postpartum hemorrhage were less common in AA patients, and the CS rate was similar [207]. Notably, there was no

increase in intrauterine death, and infants were less likely to be small for gestational age. Preterm birth in Columbia is 12% [219, 357].

The risk of appendiceal perforation increases with gestational age, and perforation in the third trimester often results in preterm labor [46]. Patients with peritonitis are more likely to deliver preterm and by CS [207]. Appendectomy in the third trimester has a 1.6× greater risk of preterm birth than in the first or second trimesters and a 3.4× greater likelihood of birth at gestational ages <33 weeks [219].

In patients with uncomplicated AA, rates of preterm delivery rate (7.7%) were within the range of the total preterm delivery rate (10.9%), while the rate of preterm delivery with MD was 26% [124]. Compared to the general rate of preterm birth of 7.7–12.3%, appendectomy during pregnancy did not significantly increase preterm delivery [37, 358, 359]. Others claim a significantly higher preterm delivery rate (10.9%) in patients with AA in comparison with normal pregnancy (4.4%) [195]. The summary of fetal outcomes is [13, 22, 26, 27, 207, 208, 219]:

- The increase in preterm delivery:
  - During the first week after appendectomy (>23 weeks gestation),
  - Age over 35,
  - BMI greater than 30,
  - Peritonitis,
- The decrease in mean birth weight at term (<3000 g or even 2500 g),
- An increase in live-born infants dying within 7 days of birth,
- An increase in APGAR <7,
- No increase in stillborn infants,
- No increase in congenitally malformed infants,
- Negative appendectomy with positive uterine pathology/inflammation carries a significantly higher incidence of fetal loss and early delivery.

In the USA (2000–2016), LA was associated with a lower preterm labor risk than OA. On the other hand, no difference in the risks of abortion

and CS between LA, OA, and conservative treatment was observed [194]. Conservative treatment was associated with a lower risk of preterm labor by 60% compared to OA [194]. Another population-based study showed that infants of patients with AA were less likely to be growth restricted at the time of birth, which is in contrast to previous reports of the increased risk of fetal weights <3000 g [22] or even <2500 g [13]. The study evaluated only patients who delivered in the context of an AA. There was no opportunity for placental insufficiency to develop or for the fetus to be exposed to the inflammatory environment and develop possible associated sequelae, such as growth restriction over the remainder of the pregnancy. If the authors had been able to follow patients who developed AA and delivered later, the fetal weight at birth would be more helpful in determining the impact of AA on intrauterine growth. Furthermore, as only 1% of pregnancies with AA were complicated by growth restriction, this raises the possibility of a coding error and missing data.

#### 15.10.4.5 Negative Appendectomy

The issue raised was the rate of increased fetal loss after the appendectomy of a normal appendix. Fetal loss rate within 30 days and preterm delivery of 2–4% for both NA and non-perforated AA was reported [208, 223, 247, 360]. These percentages are even lower than in the non-operated pregnant population [361–363]. Therefore, it is questionable that NA causes adverse perinatal results [176, 247]. Long-term follow-up after an appendectomy did not increase perinatal and intrauterine deaths in the total (normal) pregnant population [45, 252]. Other studies have limitations because only fetal demise and early delivery occur during the hospitalization for appendectomy.

The same percentage in NAR and simple AA can be explained by other inflammatory causes (15%) found with NA [208, 360]. Also, some studies did not exclude patients with a previous history of (multiple) spontaneous abortions as confounding factors.

The underlying (inflammatory) pathology, not (the type of) procedure, influences fetal risk rates. Without other pathology during NA, there is no increase in the fetal loss rate.

If there was an effect of surgical trauma on the fetoplacental-uterine elements, it should have ceased approximately 1 week after the appendectomy of uncomplicated cases [22, 27]. In one study with NA, those without further surgery were considerably more likely to continue their pregnancy undisturbed than those who proceeded with appendectomy (89% versus 57%, respectively) [244]. The week following surgery, this increased risk of delivery was present when performed after 23 weeks of gestation [26]. Any complication and increased risk of preterm delivery after that period in a patient without surgical complications should not be related to the operation itself [22, 27]. The premature delivery rate was often omitted in reports on AA, but it ranges from 15–45% [21, 108, 364]. It is now believed that subclinical IAI is a cause of preterm premature rupture of membranes or preterm labor and, as such, contributes to the leading cause of infant morbidity and mortality complications from prematurity (see Chap. 4).

There are still conclusion issues [360]. First, some authors included adverse perinatal outcomes after 30 days post-surgery. Many patients had a history of previous multiple spontaneous abortions and should be excluded from this analysis. Second, without intraoperative pathology, the patients' abdominal pain could indicate a pregnancy-related complication that caused the fetal demise. Third, in pregnant patients who underwent an NA, the percentage of LA was greater than in those with inflamed or perforated AA, which may account for this observation. Fourth, NA was present most frequently during the first trimester. Generally, the incidence of miscarriage is highest in the first trimester (10–15%) than in the 2nd (up to 5%) or third trimester (<1%) [365].

#### 15.10.4.6 Open Vs. Laparoscopic Approach

Spiros et al. conducted one of the first studies on LA influence on fetal outcome in 1987. All pregnant patients were in the first trimester, with no fetal losses [5]. All four systematic reviews [366] reported a significantly higher fetal loss rate after LA than OA but included a different number of studies. However, all four systematic reviews reported that a survey by McGory et al. [208] predominantly affected the result because of its size. It included more than half of the total participants in all studies. That study is database-related with many limitations. Fetal loss in all four systematic reviews indicated that only McGory et al. have shown that LA is significantly worse than OA for fetal loss. The remaining studies have shown no significant difference between the two operative approaches for this outcome.

LA does have a higher fetal loss rate than OA [366–368].

#### 15.10.4.7 Conversion from Laparoscopic to Open Approach

Caution should be present because of the small number of patients that have undergone such conversions [369]. Theoretically, if the conversion is indicated, then mostly (1) the anatomy is complex, or (2) the inflammation is advanced in the form of perforation or an abscess. Both situations result in a longer operative time and a higher incidence of uterine manipulation, potentially leading to a higher rate of complications. Current studies show a low (1%) rate of conversion to laparotomy that is better than most published rates of nonpregnant patients [223]. It may reflect that the LA in pregnancy is usually performed by experienced surgeons [223, 224]. The conversion rate to the open approach is 14%, associated with 50% of preterm labor and no fetal loss [235, 370].

#### 15.10.4.8 Long-Term Outcome

In most reports, the length of fetal follow-up is not defined or stated as “uneventful” [222]. Even with follow-up, no specific tests for child development were mentioned [354]. LA in pregnancy is safe and efficacious, without any long-term effects on the fetus or resulting child [371]. Studies with both laparoscopic and OA did not find developmental delays in children up to 9 years old, regardless of the trimester [227, 372]. Children may demonstrate the acquisition of developmental skills at varying rates. However, all children had a normal motor, sensory, and social development by age 3. No long-term fetal effects were noticed on gravid ewes after CO<sub>2</sub> pneumoperitoneum [389].

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## Abstract

The most common causes of gallbladder disease in pregnancy are gallstones and biliary sludge. In pregnancy, the incidence of gallbladder disease is 0.05–0.3%, and asymptomatic gallstones occur in 3.5–10% of all pregnancies. Acute cholecystitis during pregnancy is one of the most common nonobstetric operative conditions, and 40% of pregnant patients with symptomatic cholelithiasis require cholecystectomy during pregnancy. Natural history and clinical examination are similar to those in the nonpregnant population. Therapeutic options are medical, open surgical, and laparoscopic procedures. Laparoscopy is increasingly used. In the advanced third trimester, conservative treatment is recommended until delivery. 1/1200 pregnancies are complicated by common bile duct stones. Common bile duct stones have been observed in 10–12.5% of pregnant women undergoing cholecystectomy and account for 7% of cases

of jaundice in pregnancy. Diagnostic workup and therapeutic management are complex and depend on the maternal status, severity of the disease, infection, duration of pregnancy, and status of the fetus. Choledochal cysts are extremely rare but rupture more frequently than in nonpregnant populations.

## 16.1 Acute Cholecystitis/Biliary Colic

### 16.1.1 Historical Perspective

Friedrich Daniel von Recklinghausen (1833–1910) found that 90% of women with gallstones have been gravid at least once. Subsequent findings by Ludwig Georg Courvoisier (1843–1918) in autopsy studies revealed that three times as many women have gallstones as men, pointing at pregnancy as one of the major risk factors for cholelithiasis [1].

## 16.1.2 Incidence

### 16.1.2.1 General Population

The prevalence of gallbladder disease in the general population differs significantly in different populations and countries. William Mayo confirmed that gallstones occur three times more frequently in women [2]. In the USA, 10–15% of adults have gallstones. In particular, 70% of Native American women older than 30 develop cholelithiasis. Mexican American women have a prevalence of 14%, with Caucasians and Black women at 4% and 5%, respectively [3]. Chilean women are at high risk of developing gallstones [4], and populations of Latin American countries have a prevalence of gallstones up to 50% in adult women [5]. In Mexico, the prevalence is 14.3%. It increases with age—up to 25% after 60 years and 33% after 70 years [6].

### 16.1.2.2 Pregnancy and Puerperium

Complications of gallstones represent the second most common non-gynecologic condition requiring surgery in pregnancy. The incidence of gallbladder disease in pregnancy is 0.05–0.3% [7–12]. Asymptomatic gallstones occur in 2.5–10% during pregnancy and 12% in the early puerperium versus 1.3% in nonpregnant controls [4, 13–15]. Approximately 60–69% of pregnant women with gallstones are asymptomatic [4, 14]. The incidence of acute cholecystitis (AC) during pregnancy is 1/1000–1/10,000 [16–20]. Approximately 40% of pregnant patients with symptomatic cholelithiasis require cholecystectomy during pregnancy [21–23]. Cholelithiasis is the cause of cholecystitis in over 90% of cases.

At least 0.8% of women with gallbladder disease underwent cholecystectomy in the first postpartum year [24]. It is estimated that more than 32,000 young, otherwise healthy women in the USA, will require postpartum cholecystectomy each year [25]. Thus, pregnancy-associated gallbladder disease is a significant problem in young, otherwise healthy women.

Despite its relatively uncommon occurrence during pregnancy, 81% of women with symptoms of gallbladder disease had their first attack within 1 year of pregnancy [26]. A higher inci-

dence of gallbladder disease (0.39%) is found in Saudi Arabia. This is attributed to (1) a high number of repeated pregnancies and (2) genetic predisposition because higher percentages (7.5%) of pregnant women harbor silent gallstones in comparison with 3.5% in Western countries [27]. There is no statistically significant difference in the gallstone prevalence rates between Mexican-born and non-Mexican-born pregnant Hispanic women in the 20-year to 49-year age group [28].

Surgical gallstone disease during pregnancy is distributed as follows: biliary colic and AC (62.7–86.3%), biliary acute pancreatitis (AP) (3–25.4%), choledocholithiasis (6.8–7.0%), and acute cholangitis (2.6–5%) [22, 29, 30].

In 1910, almost half (10/25) of patients presented during puerperium [31].

## 16.1.3 Risk Factors

Pregnancy may constitute a defined period of subclinical metabolic stress with full clinical presentation revealed later. For example, pregnant women with gestational diabetes mellitus (DM) or high blood pressure are at risk of developing DM or hypertension [32, 33]. A similar phenomenon may happen with gallbladder sludge and stones [24].

### 16.1.3.1 Biliary Sludge

Biliary sludge, or microlithiasis, is a mixture of granules of cholesterol and calcium bilirubinate crystals up to 2 mm in diameter within viscous bile. Larger clusters are defined as gallstones on ultrasound (US). Although not sludge becomes gallstones, sludge is the initial step in gallstone formation and the earliest recognizable stage of lithogenesis [34].

Biliary sludge forms in 11–31% of women during pregnancy and gallstones form in 2–6% [4, 35–37]. New sludge or stones were found in 30% and 2% of the women at the end of their pregnancies. The postpartum US revealed the disappearance of sludge in 61% and the disappearance of stones in 28% [37]. After delivery, the disappearance of gallstones correlated with a smaller stone diameter and increasing age [37].

Therefore, some patients with symptomatic cholelithiasis during pregnancy may not have it after delivery [36]. These results should be taken with caution because the sensitivity of US for microscopic sludge is 50–60% [24]. All detected gallstones were <10 mm [4, 35].

### 16.1.3.2 Multiparity

Multiparity is a risk factor due to hormonal changes that directly influence gallstone formation [35, 38]. Pregnancy increases the prevalence from 1.3% in nulliparous women to 12.2% in multiparous [39]. Approximately 5.1% of women develop gallbladder disease after one pregnancy, 7.6% after two pregnancies, and 12.3% after three or more pregnancies [24, 40–42]. After accounting for the number of children, 12 months of breastfeeding reduces the risk of gallbladder disease in parous women by 7% [43]. The protective effect of breastfeeding could be from decreased estrogen levels during lactation [44]. However, other hormonal changes that occur with lactation may also have an effect. Early marriage and repeated pregnancies until menopause increase the probability of gallstone disease in pregnancy. A cross-sectional study found the following incidence of gallstones: in the 21- to 30-year age group, 1.4% in patients having no pregnancy, 9.6% in patients having one pregnancy, 7.1% in patients having two pregnancies, 6.0% in patients having three pregnancies, and 3.3% in patients having four and more pregnancies; in the 31- to 40-year age group, 0.6% in patients having no pregnancy, 1.4% in patients having one pregnancy, 6.0% in patients having two pregnancies, 8.2% in patients having three pregnancies, and 12.6% in patients having four and more pregnancies; in the 41- to 50-year age group, 0.8% in patients having no pregnancy, 0.6% in patients having one pregnancy, 4.4% in patients having two pregnancies, 4.4% in patients having three pregnancies, and 12.9% in patients having four and more pregnancies; and in the 51- to 60-year age group, 0.6% in patients having one pregnancy, 1.1% in patients having two pregnancies, 2.5% in patients having three pregnancies, and 14.3% in patients having four and more pregnancies. The risk of gallstone disease increases

with parity, particularly among younger women [45]. Valdivieso et al. found that 12% of women immediately after delivery had gallstones compared to 1.3% nulliparous group [4]. The increase in progesterone secretion, which remains high during the second and third trimesters, leads to smooth muscle relaxation and gallbladder dilation and stasis [46]. The incidence of gallbladder disease in the asymptomatic category was higher in patients of higher age and parity [31, 47]. Young patients with a higher parity are more prone to gallbladder disease [15, 47].

On the contrary, some claim no effect or reduced prevalence by a factor of 40 compared to nulliparae [14, 48] and that the female-specific factors of prior pregnancy and the number of previous pregnancies did not show a measurable influence on the prevalence of gallbladder stones [49]. Multiparity could be misinterpreted as a risk factor instead of age because several pregnancies sometimes include more than 10 years.

### 16.1.3.3 Diabetes Mellitus, Obesity, and Bariatric Surgery

The risk of forming gallbladder sludge or stones during pregnancy is significantly higher in obese (2.3% vs. 0.4% [12]) women (BMI  $\geq 30$  kg/m<sup>2</sup>) [7, 24]. Overweight and obesity are observed in 66% of pregnant and postpartum patients [50]. Insulin resistance, which increases with BMI, is one possible mechanism linking obesity to gallstones [51–57]. Women who formed gallbladder sludge or stones were significantly more insulin-resistant. Autopsy studies [41, 55] and epidemiological studies in Mexican Americans [51] and Caucasian Americans [42] have shown DM to be a significant risk factor for gallstones. The independent risk factor for incident sludge or stones is prepregnancy BMI  $>25$  kg/m<sup>2</sup> [24, 58]. As the prevalence of overweight and obesity in young women increases [59], pregnancy-associated gallbladder disease may become a significant problem.

Despite recognizing weight loss procedures as risk factors for cholelithiasis [10], the impact of gestation on the occurrence of biliary disease after bariatric procedures is vague. The reported incidence of symptomatic cholelithiasis in the

general population following bariatric surgery is up to 15%, depending on the procedure [60]. The cholecystectomy rate following LAGB, RYGB, and SG is 6.5%, 9.7%, and 10.1%, respectively [61].

#### 16.1.3.4 Oral Contraceptives

See Sect. 16.1.4.1.

#### 16.1.3.5 Age

Age (see Sect. 16.1.2.1) and multiparity (see Sect. 16.1.3.2) are interrelated risk factors for gallbladder disease in pregnancy.

#### 16.1.3.6 Gallbladder Volume and Function

During pregnancy, gallstone and biliary sludge formation may be related to increased fasting gallbladder volume [62] or postprandial gallbladder volume [63, 64]. The third mechanism is that gallstone and biliary sludge formation during pregnancy could be attributed to gallbladder motility dysfunction [65, 66]. A direct relationship between gallbladder hypomotility and gallstone and biliary sludge formation during pregnancy has been shown in a group of healthy pregnant women [35].

### 16.1.4 Pathogenesis

#### 16.1.4.1 Estrogens/Progesterone

Cholesterol gallstones are more common in women than men, and this gender difference begins during puberty and continues through the childbearing years [5, 67]. Pregnancy is associated with an increased percentage of colic acid, increased cholesterol secretion, increased bile acid pool size, decreased enterohepatic circulation, and decreased levels of chenodeoxycholic acid [68].

#### Progesterone

The progesterone-induced smooth muscle relaxation of the gallbladder reduces gallbladder emptying and promotes bile stasis [69, 70]. Progesterone also reduces bile acid secretion and increases the risk of cholelithiasis and subse-

quent AC [71]. The US in pregnant women shows a decrease in the gallbladder emptying rate and increased fasting and residual gallbladder volumes after emptying in the second and third trimesters. Also, incomplete postprandial gallbladder emptying is present in pregnant women [63, 66, 72].

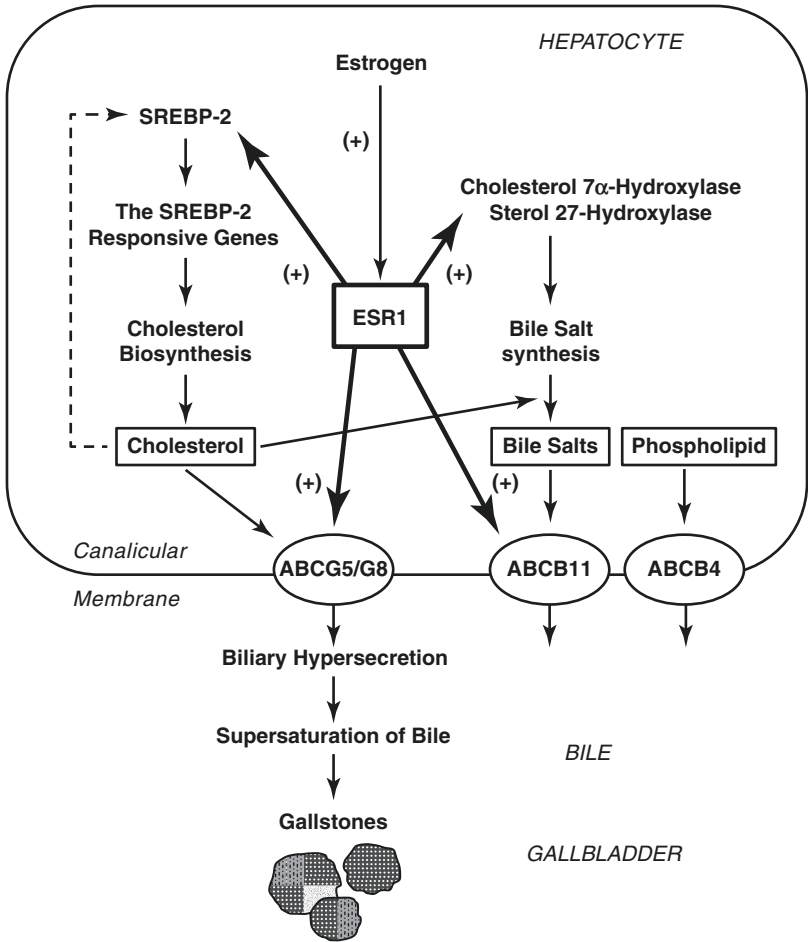
#### Estrogen

Estrogen increases the risk of forming cholesterol gallstones by promoting the hepatic secretion of biliary cholesterol that induces an increase in cholesterol saturation of the bile [73–76]. Also, high estrogen levels significantly enhance the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme in hepatic cholesterol biosynthesis even under high dietary cholesterol loads [76, 77]. Furthermore, estrogen could augment the capacity of dietary cholesterol to induce cholesterol supersaturation of the bile [77, 78], and high doses of estrogen augment intestinal cholesterol absorption [78]. During estrogen treatment, cholesterol is synthesized despite its excess availability from the high-cholesterol diet. Loss of negative feedback regulation of cholesterol biosynthesis results in excess secretion of newly synthesized cholesterol and supersaturation of the bile that predisposes cholesterol precipitation and gallstone formation [76]. Therefore, the most common type of stone in pregnancy is yellow cholesterol stones [5, 24]. Additionally, high estrogen levels induce gallbladder hypomotility [79] and sphincter of Oddi hypomotility [80]. Since plasma hormone concentrations increase linearly during gestation, the highest risk of gallstone formation is in the third trimester of pregnancy.

Also, estrogen could decrease plasma low-density lipoprotein (LDL) cholesterol and increase plasma high-density lipoprotein (HDL) cholesterol [81, 82]. The decrease in plasma LDL results from increased hepatic LDL receptor expression, which increases the clearance of plasma LDL. Therefore, the increased uptake of LDL by the liver may result in increased cholesterol secretion into the bile. These alterations could induce an apparent increase in hepatic out-

put of biliary cholesterol derived from circulating lipoproteins such as HDL and LDL. However, LDL cholesterol could have a more negligible effect on biliary secretion. Figure 16.1 illustrates the potential lithogenic mechanisms of estrogen through the ESR1 pathway in the liver. There is a high gallstone/sludge dissolution rate in the first month after delivery [84, 85]. The rate of disap-

pearance of gallstones and biliary sludge is 15–28% and 39–68%, respectively [37, 86]. After delivery, the spontaneous disappearance of gallstones is significantly more frequent in older women [37]. Speculation is that small gallstones are ejected from the gallbladder during the postpartum period when gallbladder contraction restores. It starts as early as 2 weeks after deliv-



**Fig. 16.1** Proposed model is underlying the potential lithogenic mechanisms of estrogen through the estrogen receptor 1 (*ESR1*) pathway in the liver. There is a possible “estrogen-*ESR1*-*SREBP-2*” pathway promoting cholesterol biosynthesis and hepatic secretion of biliary cholesterol in the liver. The negative feedback regulation of cholesterol biosynthesis (as shown in a dashed line) is inhibited by *ESR1* activated by estrogen, mainly through stimulating the activity of sterol regulatory element-binding protein-2 (*SREBP-2*) with the resulting activation of the *SREBP-2* responsive genes for the cholesterol biosynthetic pathway. Consequently, these alterations induce

excess secretion of newly synthesized cholesterol and supersaturation of the bile, predisposing cholesterol precipitation and gallstone formation. Moreover, the hepatic *ESR1* activated by estrogen could stimulate ATP-binding cassette (*ABC*) transporters *ABCG5* and *ABCG8* on the canalicular membrane of the hepatocyte and promote biliary cholesterol secretion. These lithogenic effects of estrogen are inhibited by the antiestrogenic ICI 182 and 780. Also, the estrogen effects on increasing cholesterol biosynthesis and promoting cholesterol gallstone formation are, in part, blocked by the deletion of the *ESR1* gene. (Reproduced with permission from [83])



ery [64] with an increased incidence of AP. In contrast, most gallstones likely remain in the gallbladder until dissolved by less lithogenic bile in older women with reduced gallbladder contractility. Thus, AP associated with pregnancy usually occurs in young postpartum women and is usually due to gallstones [37].

#### 16.1.4.2 Insulin

Apart from hormones, insulin resistance is also responsible for gallstone formation. The exact mechanisms are not clear. Cholesterol is the primary constituent of gallstones formed during pregnancy. Cholesterol gallstone formation requires several pathogenic factors, including supersaturation of hepatic bile with cholesterol and altered gallbladder motility. Hyperinsulinemia and insulin resistance may affect either of these factors. Hyperinsulinemia increases cholesterol synthesis via the HMG-CoA reductase [87] and increases the hepatic uptake of LDL cholesterol [88]. Insulin resistance is also associated with lower serum HDL cholesterol levels, a known risk factor for gallstones [89]. Administration of insulin in DM increases biliary cholesterol saturation [90].

Biliary cholesterol saturation is higher in patients with type II DM than in controls [91, 92]. Insulin inhibits basal and cholecystokinin-stimulated gallbladder motility, and gallbladder dysmotility is frequent with type II DM [93, 94]. In animal models, nonobese diabetic mice have diminished gallbladder contractility and rapid formation of cholesterol crystals [95], while gallbladder contractility correlates inversely with glucose and insulin levels in obese animals [96]. Insulin resistance is associated with gallbladder dysmotility in nonobese, nondiabetic humans [97]. Therefore, even in the absence of obesity, insulin resistance may lead to gallbladder sludge and stone formation, either by causing gallbladder dysmotility or altering biliary lipid secretion. Insulin resistance may be a surrogate for other undefined pathophysiologic mechanisms that lead to gallstone formation rather than a direct underlying cause [58].

Diabetics have an increased cholesterol saturation index in the bile compared with nondiabet-

ics [98]. Also, gallbladder fasting volumes are larger, and gallbladder motility is diminished in non-insulin-dependent diabetics compared with nondiabetics [99, 100]. Hyperinsulinemia is characteristic of noninsulin-dependent DM due to insulin resistance, and there is an association between hyperinsulinemia and an increased prevalence of gallbladder disease [51, 53, 54]. Both hyperglycemia and euglycemic hyperinsulinemia inhibit CCK-stimulated gallbladder motility [93]. Hyperinsulinemia may also be a key factor because insulin regulates the  $\text{Na}^+\text{-K}^+$  pump, adversely affecting smooth muscle cells' ionic and osmotic homeostasis, including gallbladder myocytes [101]. The  $\text{Na}^+\text{-K}^+$  pump of presynaptic nerve terminals is also regulated by insulin [101]. Moreover, decreased  $\text{Na}^+\text{-K}^+$  pump activity can increase intracellular  $\text{Na}^+$ , increasing the  $\text{Na}^+\text{-Ca}^{2+}$  exchange, thereby increasing intracellular calcium. Increased intracellular calcium will alter both smooth muscle tone and the release of neurotransmitters. Moreover, the gallbladder myocytes from obese, diabetic mice are foreshortened and respond poorly to cholecystokinin (CCK) [102].

Insulin resistance or DM may also affect alterations in the density or sensitivity of acetylcholine or CCK receptors or prevent neurotransmitters from accessing their receptors. To form advanced glycation end products, sugars can react nonenzymatically with amino groups in proteins, lipids, and nucleic acids [103]. These products cause covalent cross-linking of the collagen and protein matrix [103]. The cross-linking of the matrix may lead to stiffening of the gallbladder wall itself, limiting its contraction, or may impair CCK egress through blood vessel basement membranes, preventing CCK interaction with neural or myocyte receptors.

#### 16.1.4.3 Diabetes Mellitus, Obesity, and Bariatric Surgery

A potential explanation for the differences in gallbladder dynamics between obese and lean individuals may be the differences in serum and, perhaps, gallbladder wall lipids [104]. As a result, the smooth muscle cell cholesterol/phospholipids ratio increases, and membrane fluidity decreases

[104]. Therefore, these obese subjects with high serum total and LDL cholesterol and triglycerides may also have high gallbladder lipids, which may play a role in gallbladder function.

The rapid weight loss associated with the bariatric procedure further increases the risk of gallstone formation due to impaired gastric emptying and enhanced bile stasis [105, 106]. Pregnancy is associated with a fourfold increased risk of cholecystectomy among reproductive-aged women after laparoscopic sleeve gastrectomy. Also, over one-fourth of the women who conceived after laparoscopic sleeve gastrectomy subsequently underwent cholecystectomy [61]. Lower gestational weight gain was the only factor associated with cholecystectomy after laparoscopic sleeve gastrectomy [61]. The prophylactic administration of ursodeoxycholic acid after surgery and strict postoperative surveillance is recommended in these patients.

#### 16.1.4.4 Other

A 50% increase in the bile acid pool is associated with a concomitant steroid-induced increase in cholesterol secretion during pregnancy. Together with replacing deoxycholic and chenodeoxycholic bile acids with cholic acid, increased volume and decreased motility of the gallbladder enhance the development of biliary stones [26].

### 16.1.5 Clinical Presentation

#### 16.1.5.1 Medical History

As early as 1911, William Mayo stated that quiescent gallstones often become active during pregnancy [2]. Symptoms of gallstone disease during pregnancy are the same as in nonpregnant patients [4, 107]. An episode of biliary pain usually begins with right upper quadrant or midepigastria pain, which may increase in severity. Biliary colic begins quite suddenly and may radiate to the interscapular area, the angle of the right scapula, or the right shoulder. It may be precipitated by a fatty meal or by consuming a large meal following a fasting period. However, biliary colic occurs in a diurnal pattern, with pain peaking around midnight. Nausea and vomiting accompany episodes of colic in 50% of

patients. Finally, 70–80% of patients will have a history of known gallbladder stones, colic attacks, and fatty food intolerance [16]. Increasing severity of colicky pain, fever, or chills (rigors) usually implies an underlying complication, i.e., AC, AP, or cholangitis. Common bile duct (CBD) stones should be suspected if persistent jaundice is present.

#### 16.1.5.2 Physical Examination

During the physical examination, several signs could be elicited:

- *Direct abdominal tenderness* in the upper right quadrant. Due to somewhat distant locations of the enlarging uterus and gallbladder, there is no significant blunting of symptoms and signs,
- *Murphy's sign* (cessation of inspiration during palpation of the inflamed gallbladder) may be elicited less frequently in pregnant patients and indicates AC [108],
- *Abdominal muscle rigidity* is present with gallbladder perforation and biliary peritonitis, but abdominal wall laxity in late pregnancy might mask the classical signs of peritonitis [109],
- *Fever* and *tachycardia* are variably present and not sensitive signs. The more advanced the disease, the more pronounced these symptoms and signs are,
- *Vomiting* and *dyspepsia* are difficult to differentiate from peptic ulcers. *Itching* is a sign of either liver disease or biliary obstruction.

Only women with prepregnancy stones experience biliary pain [37].

### 16.1.6 Differential Diagnosis

Many diseases present with pain in the upper right abdominal quadrant. However, most of them could be excluded with good history taking and clinical examination. The list of the most common differential diagnoses is presented in Table 16.1.

**Table 16.1** Differential diagnosis of right upper quadrant pain in pregnancy

| Jaundice <sup>a</sup>          | No jaundice                               |
|--------------------------------|-------------------------------------------|
| CBD stones                     | Diaphragmatic myocardial infarction       |
| Hepatitis                      | Acute appendicitis                        |
| Intrahepatic cholestasis       | Pancreatitis                              |
| Preeclampsia–eclampsia         | Symptomatic/perforated peptic ulcer       |
| HELLP syndrome                 | Pyelonephritis/nephrolithiasis            |
| Acute fatty liver in pregnancy | Radiculopathy                             |
| Hepatic malignancy             | Herpes zoster (shingles)                  |
| Cholangitis                    | Perihepatitis (Fitz-Hugh–Curtis syndrome) |
| Hepatic vascular engorgement   | Rib fracture/costal margin pain           |
| Hepatic hematoma               | Pleural effusion                          |
|                                | Pneumonia                                 |
|                                | Colon cancer (hepatic flexure)            |

<sup>a</sup> Jaundice in these conditions is not obligatory

#### 16.1.6.1 Hyperemesis Gravidarum

Hyperemesis gravidarum is intractable nausea and persistent vomiting associated with weight loss greater than 5% of prepregnancy body weight and ketonuria [110]. It occurs in 0.5–1.5% of pregnancies [110] and is more common in nulliparous than in multiparous women prone to cholelithiasis and cholecystitis [111]. Hyperemesis gravidarum leads to dehydration, and hospitalization is usually required for IV fluid therapy [111]. This disorder presents early in the first trimester of pregnancy. As a rule, symptoms resolve before the second part of pregnancy, regardless of therapy. Jaundice is uncommon and, if present, is not associated with abdominal pain or fever.

Abnormal liver tests are common, but the exact frequency is unknown. A frequency of 16% has been found [112]. The most striking abnormality is the elevation of aminotransferases with ALT levels exceeding AST levels, usually in non-alcoholic and noncirrhotic liver diseases [112]. ALT levels are variable, and hepatitis serologies are helpful in the differential diagnosis, especially when ALT levels are above ten times the normal upper limit or when it is the first affected pregnancy. The associated drug liver injury should be checked, especially when jaundice is

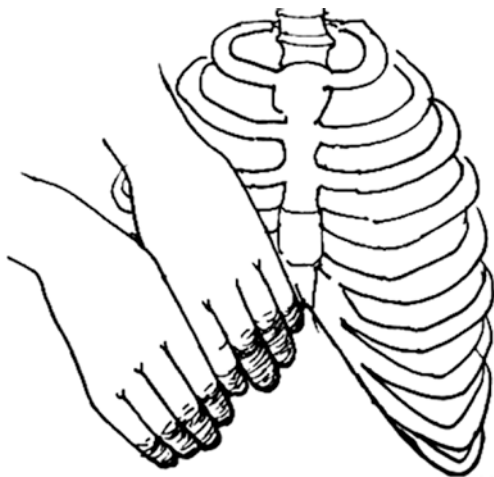
present. A liver biopsy is not needed. Pregnancies complicated by hyperemesis gravidarum have been associated with transient hyperthyroidism, which usually requires no specific therapy [111].

#### 16.1.6.2 Perihepatitis (Fitz-Hugh–Curtis Syndrome)

Perihepatitis results from early bacteremic or retroperitoneal lymphatic dissemination of *Chlamydia trachomatis* or gonococcal pelvic infection [113]. The syndrome is most frequently seen in young women and is more common in the second and third trimesters and puerperium. Inflammation in the right upper quadrant produces perihepatic adhesions. Classically, there is a sudden onset of sharp right upper quadrant pain, often pleuritic in quality. Nausea and hiccups are occasionally noted. Physical findings include tenderness under the right costal margin, occasional hepatic friction rub, and fever. Pelvic examination may be normal or may reveal signs of cervicitis or pelvic inflammatory disease. Liver function tests and cholecystogram may be transiently abnormal. A history of recent pelvic infection suggests the diagnosis, but the syndrome can be a sequela of latent or asymptomatic infection. The diagnosis is further supported by the isolation of gonococcus on cervical culture and the improvement after appropriate antibiotics [113]. Other causes should be excluded because this syndrome has no specific diagnostic marker.

#### 16.1.6.3 Costal Margin Pain

In 1921, Alexander Tietze first described a syndrome characterized by a painful affliction of the costochondral cartilages (the area between the ribs and costal cartilages) [114]. The cause of the pain is recurrent, repetitive irritation of the intercostal nerves, not synovitis of the interchondral cartilage. These factors support the hypothesis that direct or indirect trauma is the cause of the syndrome. Costal margin pain and tenderness due to stretching of muscular attachments are not uncommon during pregnancy. Upon physical examination, the pain is produced when the rib margins are displaced upward and anteriorly; thus, the *hooking maneuver* can be used to corroborate the diagnosis (Fig. 16.2). *Carnett's sign* can be used for confir-



**Fig. 16.2** Schematic illustration of the hooking maneuver. The fingers are hooked beneath the costal margins, displacing them upward and anteriorly

mation. The patient is asked to lift the head and shoulders from the examination table to tense the abdominal muscles. An alternative is to ask the patient to raise both legs with straight knees. A painful, positive test increases the likelihood that the abdominal wall, not the abdominal cavity, is the source of the pain. If a conduction block is used for diagnostic purposes, another block may be performed using long-lasting local anesthesia with 0.5% bupivacaine. After delivery (ideally breastfeeding), a combination of local anesthesia 0.5% bupivacaine and 40 mg triamcinolone (FDA class C) can be used. This has been found to relieve the problem unless further trauma recreates the pathology. Repeated local anesthesia steroid blockade may be performed if residual pain persists or reoccurs.

## 16.1.7 Diagnosis

*Pregnancy is comparatively seldom complicated by jaundice. Notwithstanding the fact that in most cases jaundice disappears without treatment, too favorable a prognosis should not be ventured, for the reason that now and again the condition may represent the initial symptom of acute yellow atrophy of the liver.*

(John Whitridge Williams, 1903)

### 16.1.7.1 Laboratory Findings

Clinically suspected biliary colic or AC should be evaluated in the hospital. Only granulocytosis (left shift) indicates a bacterial infection. C-reactive protein (CRP) is elevated, and bacterial infection is expected with values >40 mg/L. Serum bilirubin and transaminases may be elevated, as in nonpregnant women. Serum alkaline phosphatase is less helpful because estrogen causes its elevation (levels may double during normal pregnancy). Serum amylase levels are elevated transiently in up to 33%. Finally, postprandial plasma levels of total bile acids progressively increase during pregnancy.

### 16.1.7.2 Transabdominal Ultrasound

Adequate transabdominal US visualization of the gallbladder in pregnancy is 95–98% [47, 115, 116]. The remaining patients, whose gallbladder could not be visualized initially, are diagnosed with chronic cholecystitis with contracted gallbladder and thickened gallbladder wall on the rescans [47]. Gallbladder sludge (see Sect. 16.1.3.1) is visible as the accumulation of bile. It is reported in up to 30% of gravid patients, with a similar proportion of women affected by the postpartum period [24]. The US in early pregnancy confirms the physiological expansion of the gallbladder and the accumulation of stones, debris, and bile. The US of the gallbladder in healthy pregnant women shows a decrease in the emptying rate and an increase in residual volume after emptying. If gallstones are the only pathologic finding, the state is defined as biliary colic. US criteria for AC include the following:

- Gallbladder calculi,
- Wall thickening (>3 mm),
- Pericholecystic fluid,
- Sonographic Murphy's sign (focal tenderness under the US transducer positioned over the gallbladder).

CBD obstruction should be ruled out because it changes the therapeutic approach. It is suspected or confirmed by the following findings:

- CBD >7 mm in diameter,
- Dilation of intra- and extrahepatic ducts,
- Gallbladder calculi smaller than cystic duct diameter.

Abdominal pain from suspected urolithiasis is better evaluated with US. Although the diagnosis of calculus is complicated by pregnancy-related hydronephrosis, the addition of the color Doppler US of the bladder to identify ureteral jets and the transvaginal US to detect stones in the distal third of the ureter helps in the evaluation [117].

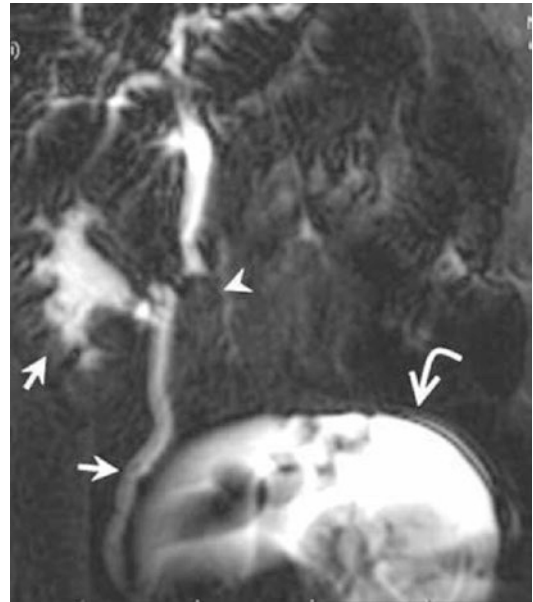
### 16.1.7.3 Endoscopic Ultrasound

See Sect 16.2.5.5.

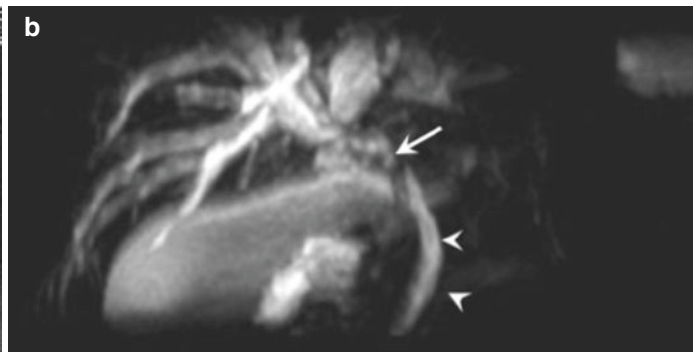
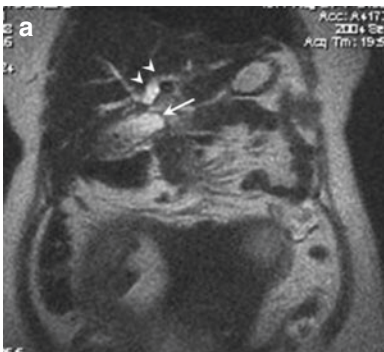
### 16.1.7.4 Magnetic Resonance Cholangiopancreatography

Magnetic resonance cholangiopancreatography (MRCP) helps differentiate CBD stones from intrahepatic cholestasis of pregnancy (see Sect 16.2.4.1) because the clinical and biochemical presentation of these two entities overlaps [118]. MRCP is indicated when dilation of intrahepatic and extrahepatic ducts (Fig. 16.3) is present on

the transabdominal US (see Sect. 16.2). It can also differentiate between CBD stones and external compression due to Mirizzi syndrome (Fig. 16.4). Additionally, the pancreas is frequently obscured by overlying bowel gas on US evaluation. MRCP better evaluates the pancreas



**Fig. 16.3** CBD stones in the second trimester of pregnancy. Magnetic resonance cholangiopancreatography shows distal common bile duct obstruction due to a calculus (arrowhead), gravid uterus (curved arrow), and physiological right hydronephrosis and hydroureter (arrows). (Reproduced with permission from [119])



**Fig. 16.4** Obstructive jaundice at 36 weeks of gestation with right upper quadrant pain. (a) Coronal T2-weighted single-shot fast spin-echo image shows distended gallbladder with cholelithiasis (arrow) and intrahepatic biliary dilation (arrowheads). (b) Thin-slice MRCP shows that the distal CBD is normal in caliber, and the inflamed and distended gallbladder compressed the common hepatic duct.

Reconstruction of thin-slice MRCP demonstrates the distended gallbladder fundus compressing the proximal CBD (arrow), causing intrahepatic biliary dilation, and a normal caliber distal CBD (arrowheads), consistent with Mirizzi syndrome. MRCP magnetic resonance cholangiopancreatography, CBD common bile duct. (Reproduced with permission from [120] under the CC Attribution License)



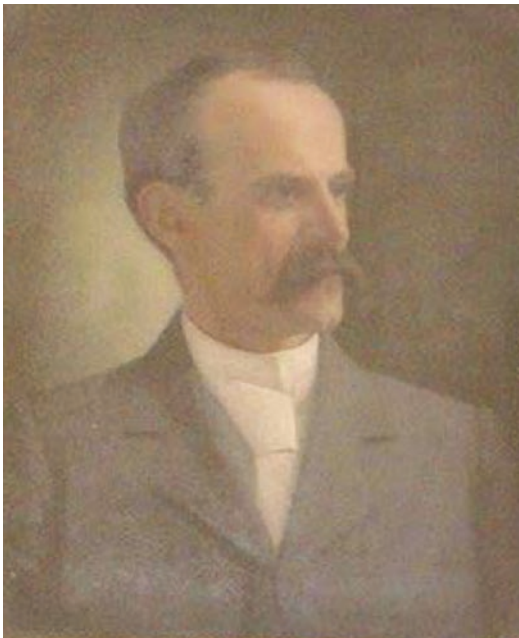
for edema, the pancreatic duct for obstruction in biliary AP, and the peripancreatic tissues for inflammation.

## 16.1.8 Treatment

### 16.1.8.1 Historical Perspective

In 1890, Robert Barnwell Rhett, Jr. (Fig. 16.5), wrote of a cholecystotomy on a pregnant woman. In 1893, Boorse mentioned a case of pregnancy complicated by the expression of biliary calculi. In 1893, Willien reported a cholecystotomy in the third month of pregnancy. In 1895, Vineberg reported two cases of AC in the puerperium and found only four previously published cases. In 1895, Davis AB reported a case of cholecystectomy in the seventh month without interrupting the pregnancy. Ploger, in 1910, gave a record of 42 cases; 22 had puerperal biliary colic, and in 19 of these, it was the first attack. The remaining 20 attributed the beginning or increase in the sever-

ity of their gallstone pains to some pregnancy [122]. Peterson collected 25 cases complicating pregnancy, including his case, and 10 complicating the puerperium. These are cases proved by operation or by finding calculi in the stool [31]. Otherwise, he could have included 20 cases of Huchard and 51 of Berline-Herwig. Since 1910, Green reported 2 cases following a miscarriage [123]; Branson, 4 cases [124]; Audebert, 1 case; and Graham, 6 cases, a relatively meager list when the frequency of gallstone operation is considered [125]. Schroeder said that 90% of operated women had borne children. Peterson found that 75% had children. Grube proves that of 657 cases of gallstone, 613 cases had children. There were 183 married and 33 unmarried or sterile women [126]. Grube concisely states that pregnancy produces changes in the biliary system: (1) stasis of the bile, (2) increase in cholesterol in the bile, (3) protein decomposition, (4) cell desquamation, and (5) hyperemia of the mucosa of the bile ducts [126]. He agrees with Hofbauer that cholelithiasis is due to the above processes plus bacterial infection and says that investigations of the liver of women who have died during or just before or after labor all of the conditions mentioned earlier are characteristic of pregnancy [127]. M’Nee and Ashoff found that some forms of stones originate in the aseptic and uninflamed bladder. M’Nee believed there is a definite relationship between gallstones and pregnancy, considering that the most common age of onset corresponds to the period of childbearing and the number of cases of gallstones in women who have borne children [128]. He believed that the pressure of the uterus causes stasis. He also found that the *cholesterme* contents of the bile were greatly increased in five women who died during, just before, or after labor. These findings coincide with those of Grube. Peterson says that in pregnancy, it is significant that in nearly one-third of the cases the period of onset is at that time of gestation when the uterus is approaching the level of the umbilicus, sending the intestines upward, and when the growing fetus is beginning to hamper the eliminative powers of the liver. In the puerperium, in one-half of the cases, the attacks occurred during the first 7 days postpartum, suggesting



**Fig. 16.5** Robert Barnwell Rhett Jr. (Huntsville, 1853–Charleston, 1901), President of the Medical Society of South Carolina and Dean of the Charleston Medical School, performed the first cholecystotomy on a pregnant patient in 1890. (Reproduced with permission from [121])

traumatism of the biliary passages during labor. He quotes Vineberg, who said the great eliminative processes going on at this period, the change in the intra-abdominal pressure, and the forced rest in bed with attendant constipation all favor these attacks.

IUoway, in 1889, reported a case of *icterus gravidarum*. The occurrence of jaundice is most important as its presence affects the uterine contents, and the nearer to the term, the greater the possibility of exciting labor. Peterson found that in 15/25 patients, jaundice was present. He stated that pregnancy could constitutionally produce jaundice without obstruction by gallstones. The operative mortality was 13% for 23 cases [31]. The pregnancy seems to have little effect. The deaths reported were from rupture of the gallbladder, empyema, or extensive or prolonged operative procedures required by the conditions found. The occurrence of miscarriage is dependent upon the pathology present more than upon the effect of the operation. In Peterson's cases, two started before the operation and three after. The latter were cases of severe infection with chills, fever, and jaundice. Graham reports a case in the sixth month where the gallbladder ruptured by a blow to the abdomen. At the operation, three gallstones were in the abdomen, one in the gallbladder, and two in the cystic duct. He gives detailed histories of four others operated upon during pregnancy, all of whom went to term. One other case refused the operation and died 2 years later from complete CBD obstruction. Regarding Graham's paper, Luiz describes a case of gallbladder rupture during labor. The patient died of general peritonitis, and 250 gallstones were found scattered through the abdominal cavity postmortem.

#### 16.1.8.2 Conservative Treatment

Up to 1997, conservative treatment was recommended [22]. Today, *uncomplicated* symptomatic cholelithiasis is mostly treated nonoperatively (82–92.5%) [129–131]. The therapy for biliary colic could be initiated or continued by a primary care physician after consultation with the gastroenterologist or abdominal surgeon. This recommendation is because even after biliary colic, there is an increased incidence of premature con-

tractions [130] and even fetal death [132]. The patients are followed up daily for several days and then once weekly. Patients with significant comorbidities should be hospitalized even for medical therapy. Traditional indication for medical therapy to delay the cholecystectomy until the second trimester when the spontaneous abortion rate after cholecystectomy is the lowest (12% in the first trimester and 5.6% in the second trimester) [133], is not recommended. Delay of surgery until the second trimester may lead to further complications of gallstone disease such as AC and biliary AP, risk of maternal malnutrition, and reduction in fetal growth rate caused by lack of maternal oral intake leading to higher spontaneous abortion rates and preterm labor (PTL) [107, 134–136]. Also, the PTL and preterm delivery (PTD) are 0% during the second trimester compared to 40% in the third trimester [133].

The only indication of conservative therapy of AC is the advanced third trimester. Cholecystectomy in the third-trimester results in a longer hospital stay, a higher cost of the cholecystectomy admission episode, and increased 30-day nonobstetric readmissions compared with women undergoing an operation in the 3 months postpartum [137]. However, the risk of PTD may be associated with antepartum disease severity and other potential causes for PTD, in addition to or instead of cholecystectomy timing [138]. Cholecystectomy during the third trimester is associated with a higher rate of PTD and overall maternal and fetal complications [138–142].

Preterm delivery rates are two- to threefold higher with cholecystectomy performed during the third trimester than up to 3 months postpartum [137, 138, 143, 144].

In patients with complicated gallstone disease initially presenting during pregnancy with operation delayed to the postpartum period, 35% recurred within 1 month, and 82% within 3 months of delivery [145]. Of those who underwent postpartum LC, up to 78.6% have recurrent attacks before the operation [129]. On the other

hand, of those who never had LC, up to 33.3% have no recurrence of symptoms [129]. Some patients with confirmed postpartum symptoms do not undergo LC. This may be due to the preference of recently pregnant patients to avoid disrupting the postpartum period by undergoing an elective operation. Furthermore, conservatively treated biliary AP during pregnancy is more likely to result in postpartum cholecystectomy [12].

Early LC in the postpartum period is warranted (giving the comfort of a nonpregnant patient) when cholecystectomy is postponed in advanced pregnancy [145].

### Total Parenteral Nutrition

Total parenteral nutrition has been an effective alternative to the surgical treatment of chronic cholecystitis in the second and third trimesters [146], with no adverse effect on maternal weight gain and fetal growth [147]. The growing fetus requires essential fatty acids and amino acids to develop and mature vital organs like the brain and lungs. Parenteral nutrition provides a viable means for the fetus to receive these supplements. A peripherally inserted central catheter (PICC) carries a lower rate of major complications and relative ease of insertion than central venous catheters. PICCs should always be considered, particularly in high-risk populations like pregnant women, considering a higher rate of minor complications like thrombophlebitis [148, 149]. PICC insertion is operator-dependent.

### Diet

A low-fat diet is essential, minimizing cholesterol-rich foods like foods of animal origin, pork, and red meat, with a slow reduction in body weight and indulging in more fruits and fiber intake. Potent natural remedies minimize the abnormal concentration of bile acids (acids that help in fat digestion), keep cholesterol levels in check, heal inflammation, clear out toxins, and eliminate excess lipids. Beetroot juice is high in fiber and has carotenoids and flavonoids that prevent cholesterol from entering the gallbladder and thus stop the formation of

solid pear-shaped gallstones. It has betaine that supports liver function and tames a high sugar level. Apple juice has a unique compound—malic acid—that helps soften and disintegrate the gallstones. A mix of raw juice comprises carrot juice, cucumber juice, and beetroot juice. The maximum concentration should be carrot juice. Cucumber juice has silica that prevents calcium stones.

### Pain Management and Antibiotics

See Chap 2.

### Anticholinergic Antispasmodics

Dicyclomine (FDA class B) passes into breast milk and could affect a nursing infant. Dicyclomine can suppress the production of breast milk in nursing mothers.

### Ursodeoxycholic Acid

Ursodeoxycholic acid, a naturally occurring bile acid agent, can dissolve gallstones by changing the composition of the bile, and it has been used in nonpregnant patients. Although ursodeoxycholic acid has been administered in pregnancy to manage ICP, its safety and efficacy for treating gallstones during pregnancy have not been established [150].

#### 16.1.8.3 Percutaneous Biliary Drainage

Pregnant patients with recurrent gallbladder colic during the first or third trimester or high-risk patients could be temporarily managed with percutaneous transhepatic gallbladder aspiration (drainage). Under US guidance and local anesthesia, a pigtail drainage tube is inserted through the liver and into the distended gallbladder. The drainage tube should remain until a fistula forms around the tube ( $\approx 2$  weeks). The major disadvantages of this procedure are bile leakage, bile duct injury, and abdominal abscess. All patients underwent LC after the procedure. It is used to postpone the operation until the second trimester or postpartum when presenting in the third trimester [151, 152]. Although patients delivered without neonatal complications and subsequently underwent LC postpartum, insufficient data prevented the recommendation of this approach [151, 152].

### 16.1.8.4 Operative Treatment

#### General Population

The early operation of AC is recommended in the general population [153] without an increased risk of bile duct injury [154, 155]. Early open cholecystectomy (OC), compared to delayed OC, had the advantages of less blood loss, a shorter operation time, a lower complication rate, and a shorter hospital stay [46]. Further, laparoscopic cholecystectomy (LC) during the first admission is associated with a shorter hospital stay, quicker recovery, and reduced overall cost than OC [154, 155].

According to the updated Tokyo guidelines [153], the severity of AC has three grades:

- *Mild (Grade I)*: Early LC is the preferred procedure,
- *Moderate (Grade II)*: Early cholecystectomy is performed. However, early gallbladder drainage (percutaneous or surgical) is indicated if patients have severe local inflammation. Because early cholecystectomy may be difficult, medical treatment and delayed cholecystectomy are necessary,
- *Severe (Grade III)*: It includes urgent management of organ dysfunction and severe local inflammation by gallbladder drainage or cholecystectomy. Delayed elective cholecystectomy should be performed later when cholecystectomy is indicated.

#### Pregnant Population

The most common indication for biliary surgery during pregnancy is repeated biliary colic (37–70%), followed by AC (20–40%), CBD stones (7%), and biliary AP in the remaining 3% [22, 135, 156]. Pregnant women with biliary AP are more likely to be treated surgically compared to other types of gallbladder disease (32.5% vs. 11.9%) [12].

There are issues in comparing nonoperatively and operatively managed groups. Nonoperatively managed group had a more complex obstetric presentation with higher rates of hypertension, pre-eclampsia, eclampsia, and gestational DM, which could have predisposed to worse clinical outcomes. However, an operatively managed group is more likely to present emergently (peritonitis

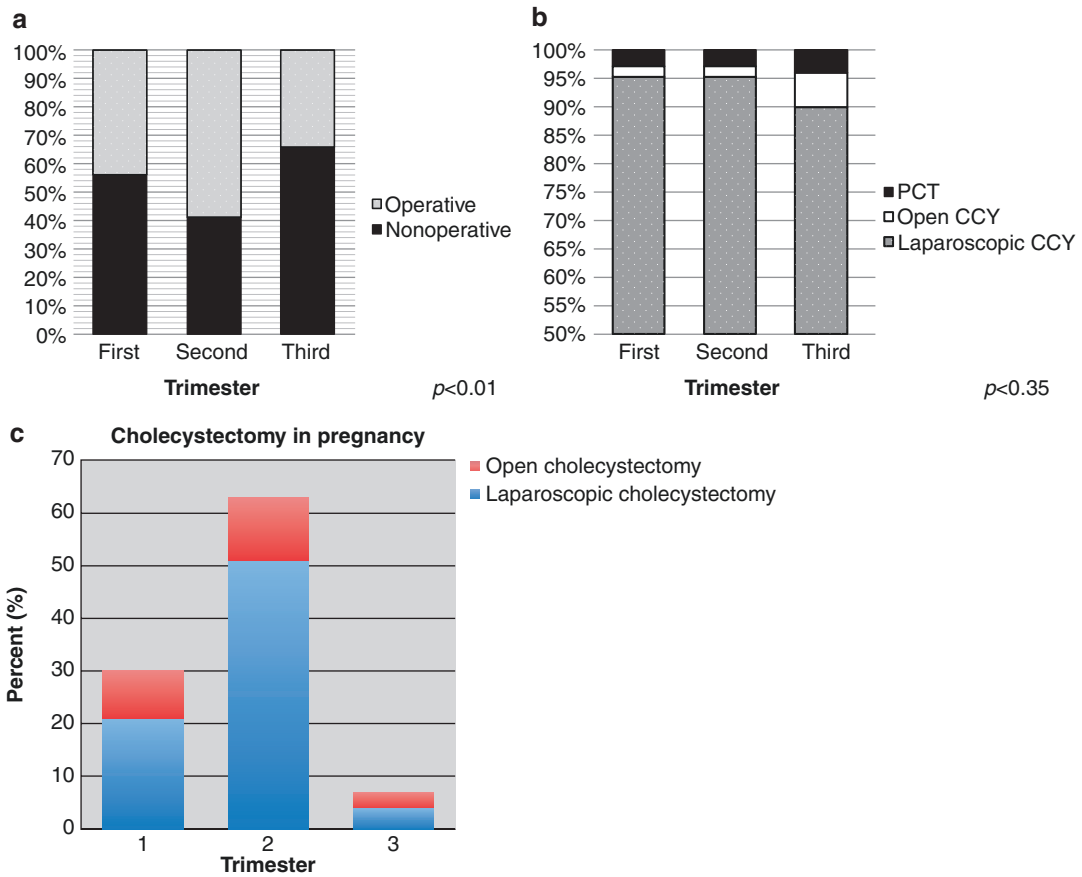
and sepsis), reflecting a higher disease severity. After accounting for such imbalances using propensity scores, patients treated nonoperatively still had higher odds of maternal–fetal complications and unplanned readmissions [142, 157].

Recurrence rates after nonoperative treatment are trimester-dependent, as high as 92% when the initial presentation is in the first trimester, 64% in the second trimester, and 44% in the third trimester [10, 132, 134, 142, 156, 158]. Some claim that the second trimester has the highest relapse rate, followed by the first and third trimesters [130, 159]. An average number of relapses during pregnancy is 2–6 [10, 30, 130, 132, 158, 160], each lasting 5–8 days [130]. Also, the disease is often more severe at relapse [130]. Contrary to current guidelines, most pregnant women admitted in the US with AC are managed nonoperatively [157].

Cholecystectomy during the first trimester does increase the risk of maternal and fetal complications compared to the second trimester [139–142]. Others claim that LC can be performed safely in the first trimester without increasing maternal or fetal complications, and there is no need to defer surgery until the second trimester [161]. The distribution of conservative and operative treatment across trimesters is presented in Fig. 16.6a. The distribution of the type of abdominal wall access is presented in Fig. 16.6b. Systematic review confirms that in advanced pregnancy, conservative treatment is preferred. If the operation is necessary, LC and OC are equally frequent (Fig. 16.6c).

LC carries a decreased risk of spontaneous abortion in the first trimester and premature contractions [133, 163] or PTL [21, 133] in the third trimester compared to OC. LC is associated with decreased risks for maternal and surgical complications [162]. Previously, LC was more common in the puerperium, while OC was during pregnancy [50]. Even in the third trimester, LC is safe without fetal morbidity [140–142, 164–169]. Today, LC for AC in pregnancy is performed in >90% in the USA [143, 157], significantly higher than two-thirds in the UK [170].

The outcomes of the third trimester should not be compared to appendectomy outcomes. Acute appendicitis and AC are distinct pathologies with different influences on uterine irritability due to



**Fig. 16.6** (a) Management strategy by trimester among pregnant patients with acute cholecystitis. (b) Surgical approach by trimester among pregnant patients with cholecystitis managed operatively. (Reproduced with permis-

sion from [157]). (c) In the third trimester, conservative treatment is preferred. (Reproduced with permission from [162]). CCY cholecystectomy, PCT percutaneous cholecystostomy tube

different (1) bacteria and localization of peritonitis, (2) distance between inflamed organ and uterus (the appendix is commonly in contact with the uterus despite trimester), and (3) incidence and speed of progression to organ perforation.

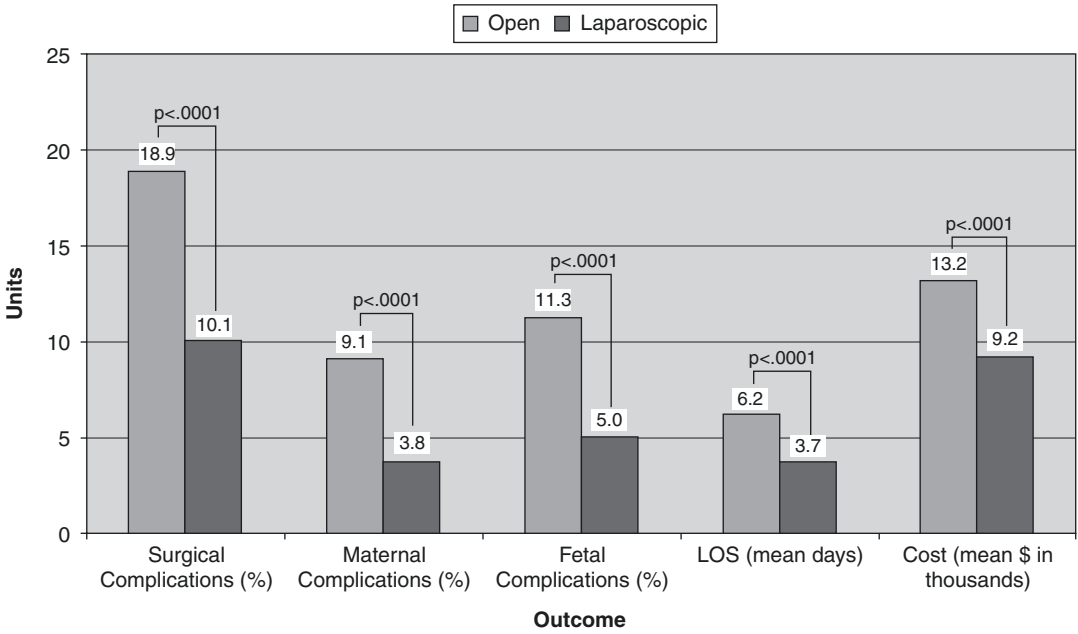
The maternal and neonatal advantages of operative treatment are [132] as follows:

- Lower consumption of medications,
- Shorter LOS and number of hospitalizations,
- Lower incidence of life-threatening complications:
  - Perforation,
  - Biliary sepsis,
  - Peritonitis,
- Lower incidence of biliary AP,
- Lower incidence of spontaneous abortions, PTL, and PTD.

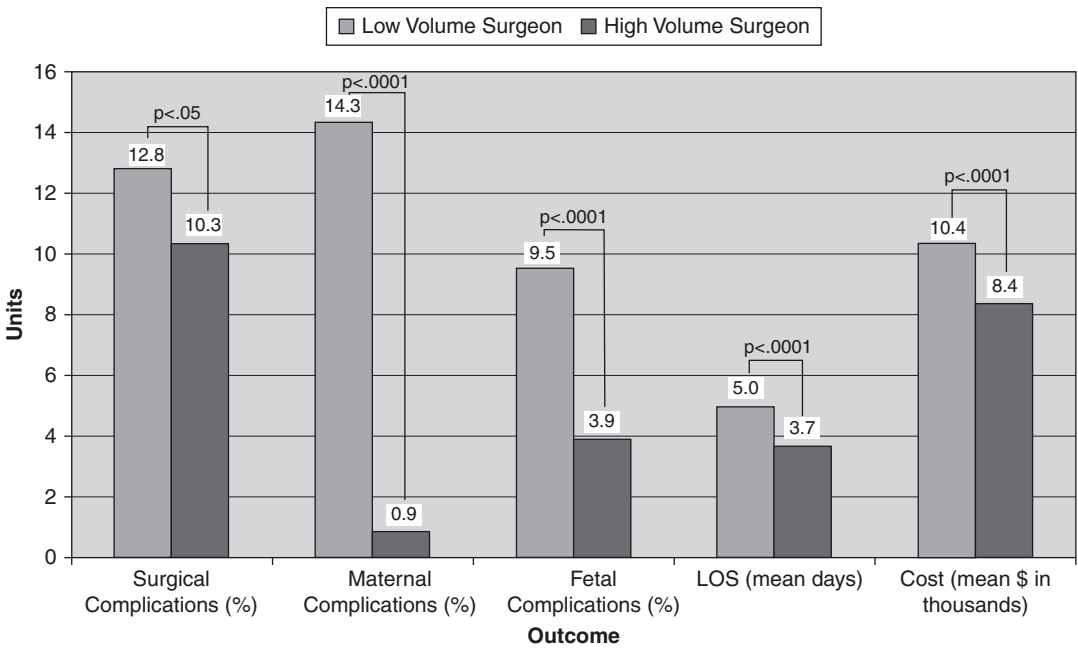
LC was performed at a mean of 5 weeks of gestation earlier than OC, and the serum alkaline phosphatase was significantly higher with the OC. No PTDs occurred after first-trimester LC in many studies [21, 168, 169]. LC has significant advantages in all outcomes compared to OC (Fig. 16.7). High-volume surgeons have better outcomes in the pregnant population than low-volume surgeons (Fig. 16.8). The conversion rate to OC in pregnancy in Australia is 13% [171].

*Laparoscopic cholecystectomy is the treatment of choice in the pregnant patient with gallbladder disease, regardless of the trimester. (SAGES Guidelines 2017 [172])*





**Fig. 16.7** Outcomes after cholecystectomy in pregnant women based on the type of procedure. *LOS* length of stay. (Reproduced with permission from [143])



**Fig. 16.8** Outcomes after cholecystectomy in pregnant women based on surgeon volume. *LOS* length of stay. (Reproduced with permission from [143])

### Contraindications for Laparoscopic Surgery

Contraindications for laparoscopy in pregnancy are principally the same as in the nonpregnant population [173]:

#### Absolute Contraindications

- Hypovolemic shock, massive bleeding, or hemodynamic instability,
- Severe cardiorespiratory disease,
- Uncontrolled coagulopathy.

#### Relative Contraindications

- Peritonitis,
- Portal hypertension,
- Multiple previous procedures/extensive intra-abdominal adhesions,
- Advanced third trimester.

### 16.1.8.5 Specific Considerations

#### Diabetic Pregnant Patient

A single article analyzed a diabetic subgroup of pregnant patients with symptomatic cholelithiasis. A total of 35.8% had DM. This is greater than in the general population of gallstone patients, among whom DM is 11.1% [174]. This may suggest that patients with DM have a greater tendency to have symptomatic gallstones in pregnancy. A more plausible explanation is that diabetic patients, educated about the tendency of DM to exacerbate the seriousness of many illnesses and already accustomed to the hospital, sought medical attention more often than nonpregnant patients. The suggestion is to perform LC during pregnancy in diabetic patients, even with biliary colic.

#### IVF Pregnancy

IVF pregnancies are constantly increasing (see Sect. 15.9.4). Therefore, the number of AC during IVF pregnancy will increase, mainly due to exposition to higher doses of female hormones, a known risk factor for the development and progression of biliary sludge and stones. Currently, there are two cases of LC in IVF pregnancy [175, 176]. There were no intra- or postoperative complications, and the postoperative recovery of mother and baby was uneventful.

### 16.1.8.6 Surgical Procedures

#### Open Cholecystectomy

Two abdominal wall incisions are used in the nonpregnant population:

- Right subcostal incision,
- Upper midline incision.

The surgical technique for both incisions is standard, found in any abdominal surgery textbook or atlas. As in any other operation during pregnancy, it is crucial to avoid or minimize uterine manipulation to minimize uterine contractions and possible PTL or spontaneous abortion. A laparoscopic [177] or standard clip applicator shortens the operative time and avoids uterine retraction. A midline incision is preferred if CS should be performed due to obstetric indications.

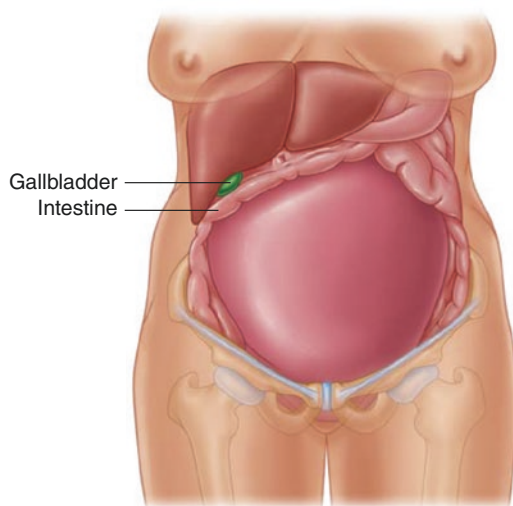
#### Laparoscopic Cholecystectomy

For principles of laparoscopy during pregnancy, see Sect. 3.2.2.2. Pucci and Seed published the first case of LC on a 31-week pregnant patient in 1991 [178].

#### Third Trimester

The previous recommendation was not to perform laparoscopy in the third trimester because of the risk of uterine injury and the intraoperative difficulties from the enlarged gravid uterus, which can obstruct safe access to the abdomen and gallbladder fossa (Fig. 16.9), and the perceived risk for excessive manipulation of the gravid uterus leading to PTL [180]. A near-term gravid uterus makes an LC technically impossible, and near-term pregnancy is the only absolute indication for OC [23, 148]. The specific problem poses patients with an indication for elective or emergent CS. After CS, depending on the severity of AC, one can decide between OC and LC and conservative treatment with elective cholecystectomy after 6 weeks.

The upper gestational limit for LC is not defined—it was set at 26–28 weeks [181], while the increasing number is successfully operated until 34 weeks [140, 168]. The location of trocar



**Fig. 16.9** Enlarged uterus in the advanced third trimester limits the working space during laparoscopic cholecystectomy [179]

placement should be adjusted according to the fundal height, earlier incisions, and surgeon's experience [182].

#### Open (Hasson) Technique

Since 2007, the *Society of American Gastrointestinal Endoscopic Surgery* (SAGES) has recommended that the initial access could be safely accomplished by (1) open (Hasson) technique, (2) Veress needle, or (3) optical trocar.

A Veress needle used for insufflation can be safely inserted in the left (Palmer's point) or the right upper quadrant in the midclavicular line, approximately 1–3 cm below the costal margin [140, 183]. After inserting a 5 mm trocar at this site, a 5 mm camera is used to guide the insertion of the rest of the ports under direct vision [140].

The usual umbilical port for the camera is placed a few centimeters cephalad from the fundus of the gravid uterus in the midline. In the first half of pregnancy, the standard supraumbilical position is used. The insufflation pressure is 12 mmHg. A pressure of 15 mmHg should not be of concern in the third trimester [140]. As the third option, optical trocars can be used with or without pneumoperitoneum under direct vision.



**Fig. 16.10** SIL cholecystectomy with a 10-mm and a low-profile, 5-mm cannula at the umbilicus. (Reproduced with permission from [185] under the CC BY 3.0)

#### Single-Incision Laparoscopic Cholecystectomy

An increasing rate of single-incision laparoscopic cholecystectomy (SILC) in the general population is translated to the pregnant population [184, 185]. In conventional laparoscopy, the open (Hasson) technique for intraperitoneal access is preferred to avoid complications from the Veress needle insertion. SILC entry is similar to the open technique eliminating the complications of blind Veress needle insertion [184]. All trocars are located through a transumbilical port eliminating an abdominal wall and uterine injury through separate stab incisions (Fig. 16.10). SILC is used during the first and second trimesters. Currently, no recommendations or guidelines for this approach in pregnancy exist.

#### Gasless Laparoscopy

See Sect. 3.2.2.2.

#### The Postpartum Surgery

See Sect. 3.2.2.2.

#### Intraoperative Cholangiography

Intraoperative cholangiography (IOC) should be used selectively. It is performed in up to 1/3 of patients [171]. Alternatives to IOC include intraoperative ductal US or choledochoscopy. However, their efficacy has not been proven during pregnancy.

### Duration of Hospitalization

LC patients could tolerate clear liquids 0.6 days sooner and regular diet 0.3 days sooner than OC patients [130]. Hospital stay is reduced by half with LC compared to OC (6 vs. 3) [133, 143, 162]. Mean hospitalization was 2–4.5 days for AC treated with LC [156, 167] and 3 days for CBD exploration [156].

## 16.1.9 Prognosis

### 16.1.9.1 Maternal Outcome

Despite the type of treatment, gallstone disease is associated with an increased risk of PTD, maternal and neonatal morbidity (including neonatal intraventricular hemorrhage and respiratory distress), and hospital readmission [12].

#### Maternal Mortality

Pregnancy does not seem to increase the severity of gallstone complications. Most (60–69%) gallstones are asymptomatic during pregnancy [4, 14, 37, 107]. Cholecystectomy in pregnancy does not increase the risk of maternal mortality [186]. Conservative and operative treatment (AP excluded) results in maternal mortality of 0% [12, 156, 187].

#### Maternal Morbidity

Pregnant women who underwent cholecystectomy compared with not operated pregnant women hospitalized with biliary tract disease had significantly lower maternal complication rates (4.3% vs. 16.5%) [143]. Following nonoperative management, the rate of emergent surgery (AC, biliary AP, acute cholangitis) is 19.5–23% [142, 158]. Compared with nonpregnant women undergoing cholecystectomy, pregnant women had higher rates of surgical complications and longer mean length of hospital stay for single hospital admission [143]. In contrast, others did not find any difference [188]. Cumulative length of stay with several relapses after nonoperative management is several fold compared to LC (see Sect. 16.1.8.4). Most complications include wound infections [156, 189], while reoperations occur up to 10% after LC [171]. No significant differ-

ence in ERCP or intraoperative cholangiogram rates, the urgency of admission, comorbidity, income distribution, hospital size, or annual volume of cholecystectomies exists [143].

### Obstetric Complications

Compared to surgical treatment, nonoperative management is associated with a significantly higher rate of labor induction and PTD requiring neonatal intensive care [130], the fetal death rate [142], and the spontaneous abortion rate [8, 107, 132]. Maternal nutrition could influence a PTL (see Sect. 4.3.4). Cesarean section (CS) rate with conservative treatment is significantly higher (35%) than with cholecystectomy [130, 131]. Older studies had a PTL rate of up to 20% after LC [36, 130, 133, 168, 190]. Currently, it is <5% [30].

#### Uterine Injury

See Sect. 16.3.

### Gallstone-Related Hospitalization During the First Postpartum Year

Gallbladder disease is a leading nonobstetric cause of hospitalization in the first year postpartum. Seventy-six percent were diagnosed with uncomplicated cholelithiasis, 16% with AP, 9% with AC, and 8% with cholangitis. Seventy-three percent of hospitalized women underwent cholecystectomy, and 5% underwent ERCP. Risk factors for hospitalization included maternal race, age, prepregnancy, overweight or obesity, pregnancy weight gain, and gestational age [7].

### 16.1.9.2 Fetal Outcome

Earlier studies on pregnancy-related gallbladder disease showed fetal loss of 12–15% [31, 158, 191], even 24% after a cholecystectomy [192]. At that time, 10% of pregnancies ended in abortion [193]. For nonoperative management, the estimated fetal mortality is 7%. Older studies had a fetal death rate after LC up to 5.2% [36, 130, 133, 168, 190], then lowered to 2.5% [142], and currently to 0% [30, 156, 171].

The causal relationship to surgery was unclear because of the varied time lapse between surgery and abortion. Cholecystectomy in pregnancy

does not increase the risk of PTL, fetal complication rates, or fetal mortality [143, 169, 186, 187, 189]. LC for the AC has no adverse effects on the fetal outcome [190, 194, 195]. Excellent cholecystectomy results for biliary colic during the second trimester of pregnancy [171] confirm that the underlying disease's severity, not the procedure itself, influences the fetal outcome. The progression to AP increases the fetal loss rate (see Sect. 16.2.7).

The first-trimester ERCP is associated with a higher rate of PTD and low birth weight [171, 196].

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## 16.2 Common Bile Duct Stones and Acute Cholangitis

### 16.2.1 Incidence

CBD stones complicate 1/1200 pregnancies [197] and are found in 10–12.5% of pregnant women undergoing cholecystectomy [159, 198], and account for 7% of cases of jaundice in pregnancy [9]. In some studies, biliary AP is the most common form, affecting up to 70% of patients with AP during pregnancy [199]. The variations in incidence result from variations in the prevalence of its most common etiologies—gallstone disease, hypertriglyceridemia, and alcohol consumption. While biliary AP complicated 1/3300 pregnancies in Dallas, Texas [200], in Southern California, 1/1500 women were affected [199].

### 16.2.2 Risk Factors

Due to the small number of these patients in pregnancy, specific risk factors are unknown. The etiopathogenesis is the same as in nonpregnant women. Risk factors are mostly the same as those for gallbladder stones in pregnancy (see Sect. 16.1.3).

### 16.2.3 Clinical Presentation

The clinical presentation of pregnant patients with CBD stones is the same as in the nonpreg-

nant population. Classic symptoms include abdominal pain, jaundice, nausea, vomiting, and itching. Painless icterus without pyrexia indicates CBD stones or periampullary tumors, while painful icterus with fever and chills points to acute cholangitis. AC can develop along with CBD stones.

The abdominal pain (colicky or stabbing) may radiate to the right flank, scapula, and shoulder. The onset of pain is rapid, with maximal intensity in 10–20 min. Pain is steady and moderate to severe. Band-like radiation of the pain to the back occurs in 50%. Other symptoms include anorexia, nausea, vomiting, dyspepsia, low-grade fever, tachycardia, and fatty food intolerance [200], some of which cannot be distinguished from symptoms of AP. Clinical presentation of biliary AP is similar to AP of any cause (see Chap. 17). The presentation of gallbladder disease can precede the presentation of biliary AP.

### 16.2.4 Differential Diagnosis

Most differential diagnoses could be excluded with an abdominal US or MRCP. The two entities in pregnancy are presented in more detail for easier definitive diagnosis: intrahepatic cholestasis of pregnancy (ICP) and acute fatty liver of pregnancy (AFLP).

#### 16.2.4.1 Intrahepatic Cholestasis of Pregnancy

##### Incidence and Risk Factors

ICP rarely occurs before 25 weeks and disappears spontaneously after delivery. The prevalence varies widely [201]. The highest frequencies have been reported in Bolivia and Chile. In Chile, the prevalence in 1974–1975 ranged from 11.8 to 27.7% according to ethnic origin [202]. For unknown reasons, the prevalence is decreasing (4.0–6.5%) [202, 203]. The prevalence ranges from 0.3 to 5.6% in the USA, according to ethnic origin [204, 205]. The prevalence in Europe is 0.5–1.5% [201]. ICP is more common in twin pregnancies [206], in winter months [207], and following in vitro fertilization treatment (2.7% vs. 0.7%) [208].



### Clinical Presentation

Pruritus is the main symptom, initially on the palms and soles, progressively spreading to other body parts and increasingly becoming more persistent. It is more severe at night and disturbs sleep. Pruritus usually disappears within the first few days following delivery [202]. The patient may also estimate pruritus intensity on the visual analog scale [209]. These scales for monitoring pruritus intensity evaluate the effect of medical treatment on this subjective symptom. The clinical examination findings are normal, except for evidence of scratching. Fever, if present, is usually caused by an associated urinary tract infection. The prevalence of jaundice varies from 17 to 75% [210–212]. Some studies may have a greater frequency of jaundice from concurrent urinary tract infections [213]. ICP with jaundice but without pruritus is rare [214]. Patients do not experience abdominal pain or encephalopathy.

### Diagnosis

Patients with ICP frequently exhibit significant increases in serum ALT activity, suggesting acute viral hepatitis, excluded by serologic tests [214]. Liver histology does not reveal necrotic lesions, and the ALT elevations may be secondary to increased membrane permeability. The serum GGT is normal or slightly increased [214]. The increased serum bile acid concentrations may be the first or only laboratory abnormality [214]. A relationship between maternal serum bile acid levels and fetal distress has been found, and evaluation of the serum bile acid concentration has been suggested for fetal assessment in patients with ICP [209]. However, no consensus has been reached concerning the usefulness of evaluating serum bile acid concentrations in the obstetric management of patients with ICP [215]. Little or no correlation has been found between the serum total bile acid concentrations and other liver test values [214]. The serum bile acid concentration and serum ALT activity decrease rapidly after delivery and, as a rule, normalize in a few weeks. The measurement of serum glutathione *S*-transferase, a maker of hepatocellular integrity, has been proposed to distinguish ICP from “benign pruritus gravidarum” [216], but its use in

routine is limited. The prothrombin time is usually normal. Abnormal values are found in severe ICP with jaundice or with cholestyramine treatment. The abnormality is caused by vitamin K deficiency, which should be anticipated and treated before delivery to prevent hemorrhage. Such therapy contributes to a good maternal prognosis. ICP is associated with preeclampsia [217] or AFLP [218] (see Sect. 16.2.4.2). US reveals no dilation of the biliary tract but may show gallstones that are unrelated to ICP. A liver biopsy is rarely necessary for the diagnosis. Histopathology is characterized by pure cholestasis, sometimes with bile plugs in the hepatocytes and canaliculi, predominantly in zone 3. Inflammation and necrosis are not usually observed, and the portal tracts are unaffected [219].

### Therapy

Apart from elective delivery, drugs used for treatment include ursodeoxycholic acid, dexamethasone, vitamin K, *S*-adenosyl-L-methionine, and cholestyramine.

### Prognosis

Most women have no lasting hepatic damage, but ICP recurs in most cases, with variations in intensity in subsequent pregnancies [206]. There is an increased risk of gallstones, nonalcoholic cirrhosis and pancreatitis, hepatitis C, and autoimmune hepatitis [220].

There is a 1–2% increase in the risk of spontaneous PTL, asphyxial events (defined as operative delivery due to asphyxia, Apgar score <7 at 5 min, or arterial cord pH <7.05), or meconium staining of the amniotic fluid or placenta and membranes for every additional  $\mu\text{mol/L}$  of maternal serum bile acids [209]. Maternal fasting serum bile acids <40  $\mu\text{mol/L}$  do not increase adverse outcomes.

#### 16.2.4.2 Acute Fatty Liver of Pregnancy

##### Incidence and Risk Factors

Harold Leeming Sheehan, in 1940, distinguished AFLP as a specific clinical entity unique to preg-

nancy [221]. The incidence ranges from 1/7000 to 1/20,000 deliveries [222–224]. The onset is usually between 28 and 40 weeks' gestation, with an average of 35 weeks [223]. It may occur during any gestation and is not always diagnosed before delivery. The risk factors are twin pregnancies [223], and 7% of triplet pregnancies are complicated by AFLP [225]. AFLP is more frequent in primiparas (70%) and pregnancies carrying a male (72%) fetus [223].

### Pathophysiology

Approximately 39% of AFLP cases are secondary to a urinary or respiratory infection [226]. The pathophysiology of the disease is obscure. The fetus' deficiency of long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) may be implicated in pathogenesis [227]. A fetus with this enzyme deficiency accumulates long-chain fatty acids that have not undergone oxidation. These fatty acids enter the mother's serum and are hepatotoxic. Furthermore, the placenta may produce excess fatty acids and further elevate maternal serum-free fatty acids (FFAs). Mothers heterozygous for LCHAD deficiency also have a greater risk of developing AFLP [227]. The long-chain LCHAD deficiency in the mitochondria determines the cell's accumulation of long- and medium-chain fatty acids. This defective enzyme is determined by a gene mutation (E47Q) [228] with an incidence of 1:150–1:200 in the population. Other hypotheses above normal (for pregnancy) levels of estrogens potentiating the effects of an otherwise tolerable hormonal insult to the mitochondria in the third trimester.

### Clinical Presentation

Most women present with a 1- to 2-week history of anorexia, nausea, vomiting, epigastric, right upper quadrant pain, headache, and jaundice [229]. In the past, jaundice was almost always present, but patients without jaundice are diagnosed because of earlier diagnosis, prompt delivery, and milder cases. The size of the liver is usually normal or small. Patients with AFLP rarely have pruritus. Hypertension and proteinuria, the main signs of preeclampsia, are found in up to half the patients [230, 231]. Patients may demonstrate asterixis and encephalopathy in

severe forms, with or without coma. Esophagitis and Mallory–Weiss syndrome related to severe vomiting and bleeding secondary to these esophageal lesions have been reported. Genital bleeding is frequent. Associated coagulation disorders exacerbate these hemorrhages. Ascites may be present. It is partially related to portal hypertension. Polyuria and polydipsia (without DM) have been noted in 5% with AFLP [230] and are almost pathognomonic in this setting. AP is a rare but potentially severe complication (see Chap. 17). Sometimes, patients present with fetal distress first, and emergent CS is indicated [232].

### Diagnosis

The serum aminotransferase levels are raised but usually not as high as in acute viral hepatitis. The bilirubin level is almost always increased. Patients may demonstrate hypoglycemia, which is uncommon in other liver diseases unique to pregnancy. In severe cases, the prothrombin time increases, and the fibrinogen level decreases. These coagulation disorders are caused by hepatic insufficiency, disseminated intravascular coagulation, or both. A low platelet count is usual in AFLP and is not always associated with other signs of disseminated intravascular coagulation. Thrombocytopenia may be the most striking laboratory feature and normalizes spontaneously after delivery. The diagnosis of AFLP should always be considered when thrombocytopenia occurs during late pregnancy and should always prompt liver function tests. Both acute renal failure, commonly acute tubular necrosis [226], and hyperuricemia are usual. The US of the liver may show increased echogenicity. An abdominal CT helps in the diagnosis. The liver density that is lower than usual may be demonstrated by Hounsfield unit values, which are equal to or lower than those in the spleen [229]. An abdominal CT is more sensitive than US, which is normal in half of the patients with AFLP [233]. These complementary examinations should not delay delivery, particularly in severe cases. Diagnosis is highly suspected on clinical grounds with routine blood tests (serum liver tests, glycemia, creatininemia, electrolytes, uricemia, full blood count including platelets, and prothrombin time).

A liver biopsy confirms AFLP, but it is not always performed because it is invasive. Also, noninvasive procedures can demonstrate fat in the liver and exclude other liver diseases, such as viral hepatitis. Nevertheless, a liver biopsy is helpful in atypical cases, particularly if the appropriate treatment (delivery) is delayed. The overall architecture of the liver is not altered. The characteristic picture is a microvesicular fatty infiltration of the hepatocytes, which are swollen. The droplets are minute and surround centrally located nuclei so that the cytoplasm has a foamy appearance. The droplets stain with oil red O, which is specific for fat. Electron microscopy confirms the presence of fat droplets [234]. A stain specific for fat or electron microscopy confirms the diagnosis in patients with ballooning cytoplasm but no evident vacuolization [229]. Therefore, whenever AFLP is suspected, a piece of the liver biopsy specimen should be reserved before paraffin embedding and processed appropriately with special stains to confirm the presence of fat in the hepatocytes. The pathologic changes reverse rapidly after delivery, and AFLP is not associated with progression to cirrhosis [231].

### Differential Diagnosis

Liver failure and derivative complications are rare with HELLP syndrome, except when spontaneous liver rupture develops (see Sect. 26.1). Patients complain of malaise (90%), epigastric or right upper quadrant pain (90%), or nausea or vomiting (50%), and some will have nonspecific viral syndrome-like symptoms [15]. Acute kidney injury is more frequent (820–100%) and profound with AFLP than with HELLP syndrome (7–36%) [235]. Hypoglycemia is almost exclusive to AFLP [235]. However, in some cases, it is impossible to distinguish AFLP syndrome from severe HELLP syndrome partially because some AFLP patients have preeclampsia.

### Treatment

The treatment of AFLP is predominantly supportive. Patients with encephalopathy may require intubation and mechanical ventilation. Profound coagulopathy may necessitate the transfusion of blood products for correction and

stabilization. Close monitoring of renal function and fluid status is of the utmost importance. Invasive hemodynamic monitoring may be necessary to assess the intravascular volumes and maintain renal perfusion.

Immediate termination of pregnancy (<24 h), emergently after maternal stabilization via the infusion of glucose and reversal of the coagulation disturbances, effectively improves the prognosis of AFLP [224, 236]. Plasma exchange combined with continuous renal replacement therapy eliminates toxins and replenishes nutrients, thus shortening the recovery time [237]. Meanwhile, the artificial liver has been used for AFLP patients [238].

Hypoglycemia is common, and glucose levels should be monitored until liver function normalizes [239]. The improvement of hepatic dysfunction heralds the resolution of the disease. Liver enzymes, ammonia, cholesterol, and coagulation begin to normalize, followed by a decrease in serum creatinine, as long as permanent damage to the renal parenchyma has not occurred. Once these measurements show improvement, serum amylase and lipase normalize [226].

### Prognosis

When AFLP was described, it was considered fatal [221], with maternal mortality up to 85% [240]. Nowadays, maternal mortality is 12.5–18% [226, 240–243], recently lowered to 4% [224]. Shortly before delivery, the recovery duration correlated with total serum bilirubin, PT, plasma fibrinogen level, and platelet counts [224].

A neonatal mortality rate was 7–66% [242, 243], recently lowered to 23–25% [226, 240, 241]. Intrauterine fetal death is attributed to placental hypoperfusion due to profound maternal hypotension. No evidence of growth restriction or phenotypic abnormalities suggests other causes [226].

## 16.2.5 Diagnosis

### 16.2.5.1 Laboratory Findings

Liver tests in pregnant women with biliary AP are frequently normal. The transaminase levels are less than 5× the normal upper limits in 89% of

patients and less than 3× the normal upper limits in 80%. One possibility is that the increased metabolism of maternal transaminases by the placenta leads to relatively normal maternal levels of liver enzymes [43].

### 16.2.5.2 Transabdominal Ultrasound

The US is the initial imaging method for evaluating the biliary system. Diagnostic accuracy for cholelithiasis is 97% [47, 115]. However, accuracy is lower for the detection of CBD (50%) and the pancreas (partial visualization in 60% with unremarkable findings) [120].

### 16.2.5.3 MRCP

MRCP is the best imaging option for biliary diseases in pregnancy if the abdominal US is not diagnostic. MRCP is rarely used due to the rarity of the disease, emergent presentation, and limited availability [120, 244, 245]. MRCP can differentiate between CBD stones and Mirizzi syndrome (Fig. 16.4). Cholecystectomy for Mirizzi syndrome improves jaundice without endoscopic sphincterotomy or exploration of the CBD. Preoperative diagnosis of Mirizzi syndrome eliminates the need for ERCP and radiation exposure. 3D MRCP sequences further improved MRCP, allowing the reconstruction of overlapping slices <1 mm. With a reported accuracy near 100% in determining the presence and level of biliary obstruction, MRCP has replaced diagnostic ERCP.

### 16.2.5.4 ERCP

#### Indications

Baillie et al., in 1990, reported the first ERCP to treat complicated gallstone disease [246]. Guidelines on AP management in the general population state that urgent therapeutic ERCP should be performed for biliary AP, cholangitis, or dilated CBD. ERCP should be performed within 72 h from the onset of pain. Patients undergoing early ERCP for severe biliary AP require endoscopic sphincterotomy [247]. However, consideration should be given to extending the therapeutic indications for emergency papillotomy to mild and idiopathic types of gestational biliary AP.

#### Timing

There is a recommendation to avoid endoscopy in the first trimester whenever possible [248]. Women submitted to ERCP in the first trimester have the lowest percentage of term pregnancies (73%), the highest risk of PTD (20%), and low birth weight newborns (21%) [196]. However, the development of hepatobiliary disease in the first trimester of pregnancy could be associated with PTD or low birth weight and not the procedure itself. The recommendation is “to intervene appropriately as early as possible.”

For radiation issues and techniques, see Chap. 1. Another issue is the risk of electrocautery use on the fetus. Amniotic fluid is a possible conductor of current to the fetus. Thus, the uterus should not be between the grounding pad and the electrical catheter. The pad should be placed higher in the posterior thoracic wall (rather than the hip). Bipolar electrocautery should be preferred to minimize this risk [248, 249].

ERCP may be the best therapeutic option during pregnancy compared to surgery or percutaneous transhepatic cholangiography.

ERCP in pregnancy tends to be safe for both the mother and the fetus. It should be restricted to therapeutic indications with additional intraprocedural safety measures [250]. ERCP should continue to be the procedure of choice for bile duct decompression in pregnancy to prevent potentially life-threatening complications to both mother and fetus [251].

#### Sedation

See Chap. 2.

#### Complications

ERCP during pregnancy is technically exacting and should be performed by experienced biliary endoscopists [68, 159, 250, 252, 253]. The complications in pregnancy consist mainly of post-ERCP AP (6–16%) [131, 196, 253], PTL, and post-sphincterotomy bleeding

[196, 249, 250, 253, 254]. There is no difference in perforation, infection, and bleeding rates of ERCPs performed in pregnant and nonpregnant women [255]. Pregnancy is an independent risk factor (OR 2.8, CI 2.1–3.8) for post-ERCP AP [255], although the pregnancy results in fewer pancreatic stents. Potential mechanisms are (1) a tendency to minimize radiation leads to more difficult cannulation, (2) the physicians could be less prone to give large volumes of IV fluid during/after ERCP or NSAIDs (nonsteroidal anti-inflammatory drugs), and (3) physiology that inherently predisposes pregnant women to PEP [255]. In uncomplicated cases, amylase normalization occurs within 36–48 h [256].

No randomized, controlled study compared ERCP with surgery regarding efficacy and safety. Also, ERCP is not the first-line treatment for CBD stones and acute cholangitis in pregnancy from choledochal cysts (see Sect. 16.3).

#### 16.2.5.5 Endoscopic Ultrasound

Endoscopic US (EUS), a semi-invasive procedure, is rarely used as a definitive diagnostic tool to identify stones in the distal CBD. EUS is appropriate before therapeutic ERCP, where non-invasive imaging such as MRCP is unavailable, contraindicated, or inconclusive. Also, it is a confirmatory tool after sphincterotomy stone extraction. Without radiation exposure, it is safe with minimal sedation-related risk. If a CBD stone is detected, an ERCP with sphincterotomy can be performed following the EUS during the same sedation.

When a CBD stone is suspected, EUS has a high positive predictive value near 100%, even for small stones  $\leq 2$  mm or sludge [257, 258]. EUS is considered the best imaging study to evaluate the CBD but requires expensive equipment, IV sedation, and technical expertise. It is superior to MRCP, an imaging method providing a large multiplanar field of view images of the biliopancreatic ductal system [259]. It reduces unnecessary interventions in patients with low or moderate probabilities for CBD stones [258].

### 16.2.6 Treatment

No consensus on the best management of biliary AP in pregnancy exists. ERCP is safe in pregnancy, and biliary stenting can be performed [260]. Previous studies have shown low rates of PTL that were not significantly different from those of conservative therapy in patients undergoing preterm surgery or endoscopic intervention for simple bile stones.

#### 16.2.6.1 Laparoscopic Cholecystectomy After ERCP

No consensus has been reached on whether LC should be performed after successful ERCP with stone extraction. There are several options.

##### Wait-and-See Approach

In one study, five patients underwent ERCP due to CBD stones, and two patients developed AC. After LC, the remainder of the pregnancy was uneventful [68]. All five patients had healthy babies at term vaginal delivery. In nonpregnant patients, the prospective randomized trial demonstrated a conversion rate of 55% in patients allocated to a wait-and-see policy after ERCP and a 23% conversion rate in the elective LC group. This result implies that LC after ERCP is mandatory (see next section).

##### Mandatory Cholecystectomy

The number of emergency department visits, recurrent biliary symptoms, and hospitalizations is significantly higher with conservative treatment than with cholecystectomy (see Sect. 16.1.8.4) or ERCP. In practice, some strongly advocate an LC within 6 weeks of the initial biliary event. In the pregnant population, ERCP is highly effective for major maternal complications [261].

The interval between ERCP and LC during pregnancy is not defined. An increased risk of conversion to OC exists 2–6 weeks after ERCP in the general population. A higher conversion rate could be that ERCP leads to inflammation around the gallbladder, including the hepatoduodenal ligament, making an LC more demanding



[262]. Adhesions, operation time, and bile duct damage were not different [262]. Others claim that time interval is of no importance. Male gender, bilirubin levels during ERCP, severe adhesions during LC, and pre-LC CRP levels were associated with an adverse outcome for an LC after ERCP.

LC should be performed 24–48 h after ERCP to shorten the hospitalization, avoid another hospitalization, and reduce the possibility of recurrent biliary events in the interval between ERCP and LC [154, 262, 263]. ERCP for CBD stones and acute cholangitis in pregnancy is preferred over the surgical approach [68, 159, 196, 246, 250, 252–254].

#### 16.2.6.2 Hybrid Laparoendoscopic Approach

As in the nonpregnant population, simultaneous (rendezvous) ERCP with LC is feasible [264]. The hybrid approach offers the therapeutic advantage of selective bile duct cannulation, decreasing the risk of complications that could be catastrophic for the mother and the fetus. Also, treatment-related costs and hospital stay would be reduced.

#### 16.2.6.3 Common Bile Duct Exploration

Although postoperative ERCP remains essential for managing retained CBD stones, routine preoperative ERCP in the general population with suspected CBD stones has declined due to low yield and an increased risk of complications and laparoscopic CBD exploration. Six cases of laparoscopic [134, 244, 262] and 20 cases of open [8, 10, 36, 130, 133] CBD explorations were described. There was no maternal or fetal morbidity or mortality. Multiple studies have demonstrated the safe and effective management of CBD stones in pregnancy with ERCP and sphinc-

terotomy with subsequent LC [36, 68, 246, 252, 262]. Therefore, indications for laparoscopic CBD exploration in pregnant patients following an episode of biliary AP are yet to be defined. Some recommend IV 1 mg of glucagon for sphincter of Oddi relaxation.

#### Transcystic Approach

In general, laparoscopic transcystic clearance of duct calculi is successful in 80–90% of and is an alternative to ERCP [262]. This approach eliminates the teratogenic effects of radiation exposure when ERCP is used during the first trimester and the inability to appropriately shield the fetus from radiation during the third trimester [254]. However, such recommendations for laparoscopic management of biliopancreatic disease to include laparoscopic CBD exploration in pregnancy are yet to be defined.

The location of the bile duct stones, size, number, and biliary anatomy should be considered when choosing between a transcystic approach and choledochotomy. Indications for a laparoscopic transcystic approach include [262] the following:

- Small (<0.8 cm) stones in the CBD,
- A limited number of CBD stones ( $\leq 5$ ),
- The absence of stones in the common hepatic duct,
- Cystic duct joining the CBD on its lateral or posterior aspect.

#### Choledochotomy

Indications for choledochotomy are [262] as follows:

- The transcystic approach fails or is contraindicated,
- Biliary lithotripsy needed,
- CBD >7 mm.

### Intraoperative Cholangiography

Since Pablo Luis Mirizzi first described IOC in 1934 [262], the technique has developed from static views to dynamic real-time fluoroscopic cholangiography and, recently, three-dimensional dynamic cholangiography [262]. In nonpregnant patients, a dynamic real-time intraoperative fluoroscopic cholangiogram is achieved with the mobile C-arm X-ray equipment, using 10–40 mL (200 mg/mL) as a contrast medium and 1 mL glucagon IV to release any papillary spasm, or in cases of DM, 1–2 mL (20 mg/mL) IV butylscopolamine. IOC with LC was described in eight reports [8, 18, 20, 36, 130, 140, 265, 266]. IOC was used frequently, along with cholecystectomy, until the early 1990s. Currently, IOC is recommended only during the exploration of CBD [140]. From these reports, maternal morbidity or mortality was nil [265].

ERCP and MRCP minimized the need for IOC. Despite the radiation exposure being in a safe range (see Chap. 1), potential risks should be discussed with the patient.

### Choledochoscopy

Choledochoscopy could be used during CBD exploration (open or laparoscopic) or after sphincterotomy. Wire-guided CBD cannulation with sphincterotomy and biliary stones or sludge removal can be performed without fluoroscopy. Choledochoscopy can confirm ductal clearance [267, 268]. If choledochoscopy is not available, an alternative approach is to use EUS-guided extraction balloon sweeps. The technique with the SpyGlass Direct Visualization System (Boston Scientific, Natick, MA, USA) is described. A 4.4 Fr sphincterotome is angled in the biliary orientation, and a hydrophilic 0.35" guidewire is gently advanced into the major papilla resulting in bile flow around the guidewire. The sphincterotome is advanced over the wire, and the aspiration of 10 mL of clear yellow bile confirmed the location within the bile duct. A biliary sphincterotomy is performed. Sweep with a 9 mm

extraction balloon is done. The SpyGlass SpyScope was exchanged over the guidewire, and cholangioscopy directly visualized the CBD, common hepatic duct, and left and right intrahepatic ducts. Saline lavage through the cholangioscope flushes debris from the CBD into the duodenum. No fluoroscopy is needed. To date, seven pregnant patients undergoing SpyGlass cholangioscopy-assisted ERCP have been reported [267–269]. The use of non-fluoroscopy interventions may prolong the overall duration of the procedure due to the learning curves and technical experiences of endoscopists and hence increase the risk, especially in complex cases. Furthermore, in daily practice, non-fluoroscopy modalities are not often used. Therefore, one should not hesitate to use fluoroscopy if required, knowing that limited radiation exposure is safe during pregnancy [250].

### Intraoperative Ultrasound

Laparoscopic US can be used instead of IOC to exclude retained CBD stones [134].

#### 16.2.6.4 Puerperium

Due to the high incidence of CBD stones in the puerperium, some recommended routine IOC even without traditional risk factors [270]. Missed CBD stones were found in 9% [270]. In nonemergent cases, MRCP eliminates radiation exposure.

### 16.2.7 Prognosis

#### 16.2.7.1 Maternal Outcome

Conservative treatment has an incidence of recurrent biliary AP of 7–70% [199], leading to severe consequences [131]. Hernandez et al. described 6 pregnant women who underwent cholecystectomies for biliary AP, with a mean hospital stay of 7.8 days and no postoperative complications, recurrence of AP, or fetal loss; 4 pregnant patients with biliary AP were clinically managed, with a 50% recurrence rate and 1 fetal loss [38].

After a single ERCP (with the complete calculi extraction), post-ERCP AP incidence is 6–16% [131, 196, 253]. When biliary drainage by ERCP is performed in the first phase, without the preoperative use of somatostatin to prevent AP, the incidence of post-ERCP AP was 2.9% [271].

As for the fetal outcome, the maternal outcome after surgical treatment is also excellent. In all 6 cases of laparoscopic and 20 cases of open CBD explorations, maternal morbidity or mortality was nil [187].

#### 16.2.7.2 Fetal Outcome

The underlying pathology influences the fetal outcome after ERCP and whether diagnostic or therapeutic ERCP is performed. The main cause of fetal mortality and morbidity is the underlying disease, not the procedure itself. One woman had a PTD out of 18 who underwent ERCP with biliary sphincterotomy for CBD stones during all trimesters [253]. At a median follow-up of 6 years, all babies were healthy. Others claim 1 AP, 2 neonatal deaths, and 1 abortion (3 months following ERCP) in 23 pregnant patients undergoing ERCP [254]. Another 17 patients in the third trimester treated by two-stage ERCP described a full-term labor rate of 67%, with 2 patients with self-limiting post-ERCP bleeding (12%) and no post-ERCP AP.

Therapeutic ERCP has a low incidence of maternal complications, prolongs gestational weeks, and reduces the induced labor rate [271]. ERCP for gallstone-induced acute cholangitis in the third trimester resulted in 66.7% deliveries at term. The risk of fetal complications related to ERCP is <5% [272]. The remaining patients delivered by elective CS because of the self-decision, not fetal distress. A trend toward a higher rate of fetal mortality (8.0% vs. 2.6%) in the conservative group suggests earlier LC (and biliary tract clearance when necessary) during pregnancy [187].

The prognosis after CBD surgery during pregnancy is excellent. Six laparoscopic and 20 open

CBD explorations resulted in zero fetal morbidity or mortality [187].

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## 16.3 Symptomatic Choledochal Cysts

### 16.3.1 Historical Perspective

Since the first pathological description by Vater in 1723 [273] and the first clinical description by Douglas in 1852 [274], more than 400 cases have been recorded in the general population. Seyffert, in 1888, published the first symptomatic case in pregnancy, when jaundice began after childbirth [275]. In 1958, Friend published the first rupture of the choledochal cyst in puerperium after normal vaginal delivery [276], and the first rupture during pregnancy was by Saunders and Jackson in 1969 [277].

### 16.3.2 Incidence

A choledochal cyst is a rare congenital abnormality of the biliary tract. The condition is reported to be common in Japan and Korea and relatively uncommon in Europe and America. One-third of the cases reported have been from Japan [278]. Incidence varies from 1:100,000–1:150,000 live births [279] to 1:13,000 births in Japan [280]. Usually diagnosed during childhood, choledochal cysts present for the first time during adulthood in 25% of patients. It is four times more common in females [279]. Until 1944, 14 cases of choledochal cysts during pregnancy and puerperium were published [281]. Up to 1978, there were approximately 50 cases of *ruptured* choledochal cysts published, in the general population, including pregnancy and puerperium [282]. Up to 2007, there was 21 case diagnosed during pregnancy and a significant number during labor and early puerperium [275, 276, 281, 283–312]. Most patients were nulliparous [303]. The Todani I type was found in 82% [303].

### 16.3.3 Pathophysiology

Choledochal cysts are an uncommon cause of obstructive jaundice, but there is a tendency to present in pregnancy [281, 283]. The cyst expansion with pain and jaundice in pregnancy may be due to hormonal effects (progesterone-induced stasis, relaxin), compression of the bile duct lumen and cyst by the gravid uterus, and increase in intra-abdominal pressure during pregnancy and labor [286, 303, 305, 309].

### 16.3.4 Clinical Presentation

Clinical manifestations are nonspecific and variable. In late pregnancy, the symptoms may exacerbate due to hormonal effects and CBD compression by the enlarging uterus [304]. The Charcot's triad (right upper quadrant abdominal pain, jaundice, and fever) is seldom in adults and one-third of pregnant patients [285, 309]. Due to anatomic dislocations during pregnancy, the cyst is not easily detected, especially in advanced pregnancy [306]. If silent, it can be unnoticed during pregnancy or found during routine abdominal US screening. Most (75%) patients present with abdominal pain in the upper right quadrant due to enlarged or palpable mass, jaundice (50%), and nausea or vomiting (50%) [303]. Complications include cholangitis, AP [284, 306], a cystic rupture with biliary peritonitis [285], and malignancy within the choledochal cyst [287]. When the biliary obstruction is present, the symptoms are similar to those of CBD stones (see Sect. 16.2). Perforation occurs mostly in the late third trimester or during labor [282], with the highest intra-abdominal pressure. Another possibility is the destruction of the cystic wall by inflammation (cholangitis) associated with biliary obstruction.

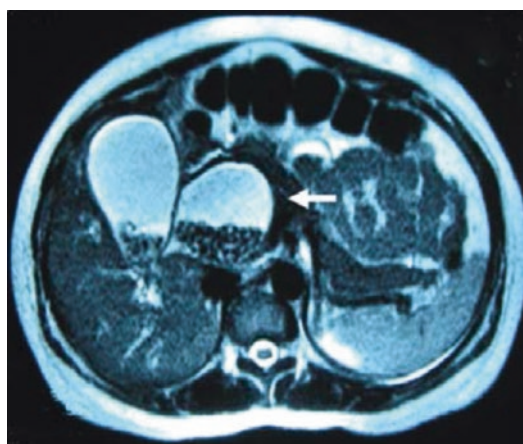
### 16.3.5 Differential Diagnosis

Due to various possible presentations, the differential diagnosis is different. When a choledochal cyst presents as obstructive jaundice in preg-

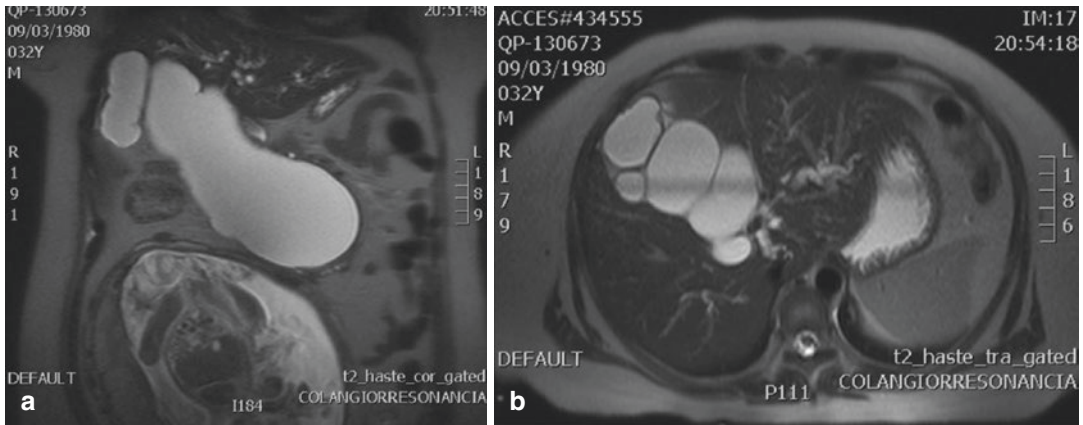
nancy, it is usually due to viral hepatitis or ICP. The most common etiologies are presented in Table 16.1.

### 16.3.6 Diagnosis

Pregnancy makes diagnosing this disease more difficult because similar symptoms are often encountered during normal pregnancy. Routine hematological and liver function tests are often of limited value. The radiographic study is limited by fetal exposure. The transabdominal US is the initial screening examination to evaluate (painful) abdominal mass, acute abdomen, or hepatobiliary conditions. However, difficulties may arise due to distortion of the normal abdominal anatomy and gravid uterus during pregnancy. The cyst may be misdiagnosed as an ovarian tumor or mucocele [311]. ERCP or CT may provide more accurate information, but ionizing radiation should probably be avoided in pregnancy [288]. MRI is the preferred method due to the high resolution of the biliary tree without the problems associated with exposing the mother and the fetus to ionizing radiation [312]. MRI can even define the type of choledochal cyst (Figs. 16.11 and 16.12).



**Fig. 16.11** MR of the abdomen at 22 weeks of pregnancy shows gallbladder calculi and choledochal cyst (white arrow) filled with calculi. (Reproduced with permission from [302])



**Fig. 16.12** Coronal (a) and axial (b) view of MR cholangiopancreatography shows a large Todani I type choledochal cyst in 22 weeks of pregnancy. (Reproduced with permission from [313] under CC BY 4.0)

### 16.3.7 Treatment

Although choledochal cysts rarely occur in pregnancy, clinicians must be aware of the condition, as delayed or inappropriate therapy may be catastrophic for both mother and child. Once the diagnosis is established, patients should be referred to specialized centers where treatment can be carefully planned due to the likelihood of cyst-related complications in the short and long term. The timing of the operation depends on the type of presentation (elective or emergent presentation), and the type of operation depends on the type of cyst according to the Todani classification. The same surgical principles in the postpartum period as during pregnancy are recommended—emergent presentation requires an emergent operation [307]. Otherwise, elective operation in puerperium or after the termination of breastfeeding minimizes postoperative complications or medication therapy related to the newborn.

#### 16.3.7.1 Asymptomatic Choledochal Cyst

An asymptomatic (palpable) mass without other symptoms should be checked regularly. Several treatment strategies exist. First, definitive treatment is postponed after labor and puerperium to minimize the influences of the operation on the mother and fetus. Second, after elective term CS,

definitive treatment of the choledochal cyst is performed in the same act. The first option sounds more logical and is recommended because during pregnancy: (a) complex surgical procedures result in a long recovery and possible complications which affect both mother and fetus, (b) hemostasis may be difficult due to a hyperemic state in pregnancy, and (c) the operative view might be obscured by the gravid uterus. There are no recommendations about timing after CS, definitive surgery 6 weeks after delivery [304, 309], or delayed definitive surgery when the patient's general physiological condition becomes normal after elective CS [304].

Indications for the semi-urgent surgical intervention of an asymptomatic choledochal cyst in pregnancy include (a) symptomatic cysts, (b) an increase in size on serial US screening, or (c) suspected/confirmed cholangiocarcinoma.

In elective settings, recommended surgical technique in pregnant and nonpregnant women is complete excision of the extrahepatic duct, cholecystectomy, and Roux-en-Y hepaticojejunostomy. Cyst excision eliminates the risk of malignant degeneration, which is as high as 30% [314], or cyst inflammation. For large cysts, bilateral Roux-en-Y hepaticojejunostomy could be performed [311]. Complete excision of the extrahepatic bile duct from the hepatic hilum to the pancreaticobiliary duct junction is the most radical solution. In some cases, it is combined



with pancreaticoduodenectomy or hepatic resection. If the structures in the porta hepatis are not identifiable, especially after repeated attacks of cholangitis leading to adhesion formation. In such cases, choledochocystoduodenostomy is performed. A side-to-side anastomosis is performed between the most dependent part of the choledochal cyst and the second part of the duodenum. The endoscopic sphincterotomy of type III cysts is the method of choice. Treatment is still controversial for type IVa cysts (combined extra and intrahepatic biliary dilation). Total cyst excision, including hepatectomy, has been recommended in general [315] and pregnant [288] populations. Concerning type V cysts, some recommend hepatic resection for unilobar Caroli's disease [316].

### 16.3.7.2 Complicated Choledochal Cyst

#### Acute Cholangitis

The complication in the form of acute cholangitis can occur: (a) as the progression of the natural history of the disease and (b) it was also described after CS possibly due to kinking of the CBD. Acute cholangitis (with or without biliary obstruction) can be treated first by percutaneous cystic decompression under US, CT, or MRCP guidance. Antibiotics should be administered. After labor and ideally puerperium, definitive excision of the cyst and a hepaticojejunostomy with Roux-en-Y reconstruction are recommended [120, 306]. In late pregnancy, elective CS followed by percutaneous decompression after 6 weeks is recommended [304]. Although no recommendations exist, some perform definitive surgery 6 weeks after delivery [304, 309].

However, complications such as AP [284, 286] or biliary obstruction [120] require a more urgent approach.

#### Choledochal Cyst Rupture

Preoperative definitive diagnosis is rare with acute abdomen due to the rarity of the disease and additional nonspecific symptoms. During



**Fig. 16.13** Intraoperative picture of the choledochal cyst with perforation in the anterior wall of the bile duct. (Reproduced with permission from [317])

exploration, the bile-stained intra-abdominal free fluid with a dilated CBD should raise the possibility of a ruptured choledochal cyst [289]. The intraoperative cholecystography [310] or transcystic cholangiography after a cholecystectomy [285] is confirmatory. Sometimes rupture is evident intraoperatively (Fig. 16.13). After detecting the condition, the initial step is thorough lavage and insertion of a T-tube. This is followed by a definitive operation that comprises the excision of the choledochal cyst with the restoration of biliary-enteric continuity. This is done electively after MR cholangiography or postoperative cholangiography [317]: (a) in the second trimester [290] when fetal complications are the least common, (b) as part of the CS in the third trimester [287], or (c) in the postpartum period [308, 317].

### 16.3.7.3 Obstetric Management

The route of delivery for a patient with a choledochal cyst is controversial. Cyst rupture due to increased intra-abdominal pressure during labor is possible if untreated. After external percutaneous drainage for cyst decompression, vaginal delivery is not contraindicated [305, 308].

## 16.3.8 Prognosis

### 16.3.8.1 Maternal Outcome

The maternal prognosis is excellent, with 90% of survival [313].

### 16.3.8.2 Fetal Outcome

Up to 2016, 30 cases without 11 fetal outcomes claimed fetal mortality of 26.3% [313]. In a review from 2007, 14% of cases with known data resulted in fetal mortality, 43% in CS, and 43% in vaginal delivery. The abortions occurred in patients with complications—biliary peritonitis, cholangitis, AP, and postoperative sepsis [303].

conservative management. Risk factors for gallbladder perforation in adults include age >60 years, immunosuppression, steroid use, and severe systemic disease [322].

### 16.4.2.2 Perforation of the Common Bile Duct

Spontaneous CBD perforation is even rarer in adults, with <50 cases reported [322–324] and 12 cases in pregnancy [319, 320, 325–333], seemingly a high number compared to the general adult population. Increased intra-abdominal pressure during pregnancy could have a role, or non-pregnant cases are underreported.

## 16.4 Spontaneous Biliary Tract Perforations

### 16.4.1 Historical Perspective

Bile duct perforation is most common in infants related to congenital biliary system anomalies. In 1882 [318], John Freeland reported the first case of an extrahepatic biliary system rupture in an adult diagnosed at autopsy. The first two descriptions of CBD perforation in pregnancy were by JT Hogan Jr. in 1957 [319] and then Maurice Abitbol, from the Jewish Hospital of Brooklyn, in 1958 [320], who was unaware of the article published by Hogan Jr. Wade Stone, in 1937, published one of the first spontaneous gallbladder ruptures in pregnancy.

### 16.4.2 Incidence

#### 16.4.2.1 Gallbladder Perforation

Gallbladder or CBD perforations as a cause of peritonitis in pregnancy have been rarely reported, and the exact incidence in pregnancy is unknown. Gallbladder perforations usually result in an abscess due to the adhesions between the gallbladder, the greater omentum, and the parietal peritoneum [321]. Although gallbladder perforation has been reported in 3–10% of adult AC cases, free gallbladder perforation into the peritoneal cavity is even rarer—in 0.5% undergoing

### 16.4.3 Pathogenesis

Apart from the pathogenesis of spontaneous biliary perforation in the adult, which is poorly understood, recognized mechanisms include (1) calculous perforation at the site of impaction, (2) calculous erosion without impaction, (3) increased canalicular pressure due to obstruction by the tumor, stone, or spasm of the sphincter of Oddi, (4) intramural infection, (5) mural vessel infarction leading to mural necrosis, or (6) rupture of a biliary tract anomaly such as cyst or diverticulum [334]. Approximately 70% are related to calculi in pregnancy [329, 335]. The obstruction leads to an increase in intraductal pressure. This leads to the dilation of the biliary tree and subsequent stasis and infection, ascending cholangitis, and thrombosis of intramural vessels. The perforation site is either at the fundus of the gallbladder [336], which is farthest away from the blood supply, or less commonly at the neck from the pressure of an impacted stone [337]. Compression or dilation at the level of CBD leads to necrosis resulting in a CBD wall perforation, commonly in the supraduodenal portion (Fig. 16.14) [332, 335, 336].

The main hypothesis of spontaneous idiopathic CBD perforation includes hemodynamic changes associated with higher pressure in the vena cava during pregnancy [328]. Increased intra-abdominal pressure could have a role because most cases present in advanced preg-



**Fig. 16.14** Perforation of the supraduodenal segment of the common bile duct (*arrow*) on the seventh day postpartum. (Reproduced with permission from [335] under CC BY 4.0)

nancy or early puerperium [335]. Balsarkar et al. reported the earliest gestation with CBD rupture at 28 weeks [333], and half of the patients are during early puerperium [335].

#### 16.4.4 Clinical Presentation

Most patients had symptomatic cholelithiasis for months or years. Such pain got relieved with analgesics. The onset is acute (20%) or insidious [335]. Perforation of the gallbladder or CBD results in a sudden onset of right-sided upper abdominal pain that becomes generalized [332] and distension [336]. Bowel sounds are absent. Insidious onset results in abdominal distention without abdominal pain and clay colored stool. Progressive jaundice may follow [335].

Physical examination reveals high-grade fever and moderate or severe dehydration, depending on the duration of the condition [336]. This is accompanied by tachycardia and normal blood pressure initially [332], followed by hypotension [336]. Icterus could be present. Abdominal examination reveals generalized

tenderness, guarding, rigidity, and rebound tenderness [332, 336]. Shifting dullness and fluid thrill are signs of large intraperitoneal quantities of bile [336].

The obstetric history of current and previous pregnancies is normal. During the early phase of the disease, obstetric status is normal.

#### 16.4.5 Differential Diagnosis

The most common include perforated peptic ulcer [332, 336], bowel perforation [336], and HELLP syndrome.

#### 16.4.6 Diagnosis

##### 16.4.6.1 Laboratory Findings

Leukocytosis over  $15 \times 10^9/L$  is common, with neutrophilia [332, 336]. Kidney and liver function tests are usually normal. With dehydration and ongoing biliary peritonitis, prerenal insufficiency is common. Elevated liver function tests raise suspicion of this condition, especially with free intra-abdominal fluid [328, 332]. Hgb is usually normal, or there is physiologic anemia of pregnancy [336].

##### 16.4.6.2 Transabdominal Ultrasound

Previously, abdominal paracentesis was helpful in the diagnosis of biliary peritonitis. Today, transabdominal US is routine imaging for hepatobiliary conditions. Depending on the duration of the condition, a large collection of fluid on the right side, in all quadrants of the peritoneal cavity, is present, mostly with distended bowel loops [335, 336]. Gallbladder with gallstone can be found, but a definite diagnosis is unclear [325, 330]. US-guided diagnostic aspiration of the collection reveals frank bile, which is confirmed by ascitic fluid/serum bilirubin ratio [330, 332].

##### 16.4.6.3 Abdominal CT

CT is rarely done due to the urgency of the condition. Also, it is rarely diagnostic. Sometimes the only finding is free intra-abdominal fluid without apparent cause [325, 335].

### 16.4.7 Treatment

If indicated, the best approach is midline laparotomy for both complete abdominal exploration and CS. Procedures depend on the location and cause of perforation. Surgical management of gallbladder perforation consists of cholecystectomy, copious irrigation, and abdominal cavity drainage [322]. The recommended treatment for CBD perforation includes cholecystectomy and CBD exploration for stones. A primary suture is not recommended, especially in the cause of perforation is unknown. The biliary tree is decompressed with T-tube drainage in cases of small perforations. Roux-en-Y biliary-enteric anastomosis is indicated for large ductal disruption [334]. CBD perforation detected during the diagnostic evaluation is treated with endoscopic CBD stent placement followed by immediate or delayed biliary surgery (if necessary) is indicated [331]. If the general or hepatobiliary surgeon is not available, subhepatic drainage with several large-diameter drains is recommended. The patient is transferred to adequate surgical facilities [328].

### 16.4.8 Prognosis

Since this condition is unusual during pregnancy and the symptoms and signs are often nondiagnostic, accurate diagnosis and treatment were delayed resulting in perinatal morbidity [322]. Peritonitis in the third trimester commonly results in PTL during the first several postoperative days [336].

Fetal prognosis is good because (1) 50% of perforations develop in the early puerperium [335] and (2) the rest mostly in the advanced third trimester. This results in a live birth with CS made during the biliary operation [325] or live birth during the term or preterm vaginal deliveries after the biliary operation [330].

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## Abstract

Acute pancreatitis (AP) is a rare entity in pregnancy, mainly caused by hyperlipidemia or gallbladder disorders. In many cases, symptoms of cholelithiasis and biliary sludge precede the presentation of AP. Diagnosis is based on clinical presentation, laboratory investigations, and modern imaging methods such as abdominal magnetic resonance imaging or magnetic resonance cholangiopancreatography. General management of mild AP in pregnancy is conservative and supportive, while severe AP should be treated in the intensive care unit. Endoscopic or surgical interventions are common. Biliary AP can be resolved with urgent ERCP sphincterotomy followed by laparoscopic cholecystectomy, preferably in the second trimester when technical conditions are optimal and risk for the fetus and pregnant woman minimal. Laparoscopic cholecystectomy can be postponed after delivery when the third trimester ERCP is done. Hyperlipidemic AP is treated with lipid-lowering methods, sometimes even with a therapeutic delivery. Immediate parathyroidectomy is indicated with primary hyperparathyroidism-induced AP. One of the

most common types, biliary AP, is associated with better outcomes than non-biliary causes.

## 17.1 Historical Perspective

Acute pancreatitis (AP) during pregnancy is extremely rare. German gynecologist Wilhelm Joseph Schmitt (1760–1827), working in Wien, reported the first case of pregnancy complicated by hyperlipidemic AP in 1818 [1] in a 30-year-old woman who died in the fourth month of her eighth pregnancy. William Lawrence (Fig. 17.1) in 1831 [2] described the second case also with maternal mortality. It is difficult to confirm whether the AP (macroscopic description without a definitive microscopic diagnosis) started during advanced pregnancy. The pregnant woman was extremely thirsty during advanced pregnancy and postpartum. The inflammation, sepsis, or possible (gestational) diabetes mellitus (GDM) could be the cause. Mondière suggested a possible association between AP and pregnancy in 1836 [3]. Lawrence later collected a series of 53 cases. German author, Marcus, collected 44 cases up to 1930 [4]. Longmade and Edmondson [5] added nine personal cases. Sheehan, in 1940, first recognized the association between acute fatty liver





**Fig. 17.1** Sir William Lawrence (Cirencester, July 16, 1783–London, July 5, 1867), son of a surgeon, helped the founding of the *Lancet* journal, was elected to the *Council of the Royal College of Surgeons* in 1828 and became its President in 1846, and again in 1855. He also became a *Serjeant Surgeon* (an officer of the Medical Household of the Royal Household of the Sovereign of the United Kingdom). (From Wikipedia)

of pregnancy (AFLP) and AP. In 1952, four additional cases were reported in France [6]. In 1955, Ross suggested a rise in intra-abdominal pressure, such as undue prolonged second stage of labor, as a pathogenesis of AP in pregnancy [7].

The first report of postpartum AP seems to be by Haidlen in 1884 [8] and other early cases by Watts [9] and Deaver [10]. Joske collected personal series of six patients with postpartum AP presentations [11].

## 17.2 Incidence

Incidence varies more significantly than in the general population (England, Denmark, and the United States: 4.8–24.2/100,000 [12]), ranging from 1/1000 to 1/12,000 pregnancies, and rarely progresses to the necrotizing form [13–19]. It is

more common in East Asian countries, including China, where AP in pregnancy accounts for 4.25% of all (unknown whether only women all both sexes are included) AP [20] or 1/441 pregnancies [21].

Accurate assessment of disease incidence in pregnancy is complex. During normal pregnancy, patients expect some degree of abdominal pain. Therefore, mild disease may be underreported. Also, there is an issue with the definition of AP in pregnancy. Some included 10 months before parturition, which ends up 10 months postpartum [22], while the standard definition of the postpartum period is 6 weeks [4]. In addition, some causes are attributed to biliary stones without definitive confirmation. Biliary sludge and gallstones exist in 10% of people in Western countries. The incidence rises in pregnancy, and it is questionable that gallbladder stones or sludge caused AP in some patients without definitive diagnostic elimination of all other causes. In some studies, nearly 70% of cases are secondary to biliary stones or sludge, followed by hyperlipidemia and alcohol abuse in approximately 20% of cases, respectively [13, 23, 24]. Therefore, the discrepancy in incidence is due to [25] the following:

- The rarity of the disease,
- The postpartum period up to 10 months,
- Different decades and countries,
- Underestimation due to underreporting,
- A small number of cases in studies,
- Multiple possible causes are not definitively excluded.

### 17.2.1 Age, Trimester, and Race

More and more women become pregnant at a more advanced age, and the incidence of AP in the general population increases with age [26]. The mean age in the two largest studies up to 1973 was 24.2 and 27 years, respectively [5]. Until 1951, primipara suffered from AP more often than multipara. The primipara is even more prone to AP if she has gallstones [5]. Current

studies show that AP is more frequent in multiparas, 64–75% [13, 27, 28].

The Hispanic population has a higher incidence (0.1%) due to a higher risk for gallstone disease [29]. Alcohol-induced AP is rare in countries, especially in the Middle East, where alcohol consumption is forbidden.

AP appears more prevalent in advanced gestation, most commonly in the third trimester [23, 24, 30, 31]. The trimester distribution depends on the population studied and varies from 19 to 28% in the first, 21 to 33% in the second, 43 to 78% in the third, and 2 to 38% in the puerperium [13, 25, 27–29, 32]. The proportion of severe AP (SAP) also fits the rule that frequency increases with gestational age (1st, 2nd, and 3rd at 0%, 11.1%, and 88.9%, respectively) with a much larger span [32]. The trimester distribution is consistent with (1) a potential lithogenic effect of estrogen during pregnancy [13, 25], (2) a physiological type of insulin resistance in the second and third trimesters of pregnancy [33], (3) a progressive physiologic increase in both serum cholesterol and triglyceride concentrations, with peak levels reached at term, in response to elevated estrogen levels, (4) possible compression effect of the uterus on a biliary tree, pancreatic vessels and pancreas itself, and (5) significant rise in intra-abdominal pressure due to prolonged second stage of labor [7].

### 17.2.2 Biliary

During pregnancy, cholelithiasis is the most common cause of AP, accounting for up to 70% of cases [13, 17, 34]. The biliary cause is also the most common in puerperium [22]. Pregnancy increases the incidence of biliary sludge and stone, which can cause AP (see Sect. 16.1.3).

### 17.2.3 Hyperlipidemia/Dyslipidemia

Chylomicronemia occurs when plasma triglyceride levels exceed 1000 mg/dL. The *chylomicronemia syndrome* is defined when chylomicronemia is accompanied by one or more of the following:

- Eruptive xanthoma (see Sect. 17.4): small yellowish papules, frequently with an erythematous base, appearing predominantly on the buttocks and elbows caused by deposition of large amounts of chylomicron triglycerides in cutaneous histiocytes,
- Lipemia retinalis (see Sect. 17.4): the retina has a salmon-colored, creamy appearance, and the retinal vessels are white,
- Abdominal findings: abdominal pain, acute pancreatitis, or hepatosplenomegaly.

The association of hyperlipidemia with AP during pregnancy was first reported in 1818 and was the first published case of AP during pregnancy [1]. Until 1970, 101 reports were published, with 15 cases between 1956 and 1996 [35]. Previously, 1.7–6% of AP in pregnancy were attributed to hyperlipidemia [36, 37]. Currently, AP secondary to hyperlipidemia/dyslipidemia has an estimated incidence of 1/25,000 births [38], or 10–56% of cases [31, 39, 40], much higher than 1–7% in the nonpregnant population [41, 42].

Failure to investigate chylomicronemia as a cause of AP leads to underestimating its incidence. First, some cases are declared idiopathic due to a lack of lipid profile testing. This confirms the importance of triglyceride (TG) levels pre-screening before initiating estrogen-related medical treatment such as IVF [43]. Second, determining the exact etiology of AP may be complicated by the role of ethanol in precipitating severe hypertriglyceridemia. The same problem with defining etiology is present in hypothyroid patients or patients with DM. Third, within 24–48 h of the onset of AP, in most patients, TG levels fall rapidly because of fasting, when the supply of chylomicrons from the intestinal absorption to the blood is cut off. Also, the therapy with hypocaloric IV fluids decreases the secretion of very-low-density lipoproteins (VLDL) from the liver, further reducing the TG pool and decreasing its levels [44]. Therefore, if the lipid profile is not checked during admission, it could be falsely negative later. Additionally, the universal mild-

to-moderate hyperlipidemia secondary to AP should not be confused with marked hypertriglyceridemia (HTG) that causes AP [45]. Whether the elevated TG is an epiphenomenon of the AP or the actual cause of the inflammation can be challenging to differentiate. The serum may be lactescent in 4–20% of the general AP population, and lipid levels increase above normal in up to 50% of patients with AP of any cause [46–50]. HTG-induced AP is equally distributed across trimesters [31]. Approximately one-third of the women developing HTG-induced AP during pregnancy were nulliparous [13, 51].

### 17.2.4 Alcohol Abuse

Idiopathic AP in pregnancy is considered alcohol-induced in 12.3–16.5 [25, 52]. Alcohol-induced AP could be even more prevalent (17.8% overall; 12.3% of 89 AP cases vs.  $\leq 7\%$  in other studies) [23, 53, 54] due to the inclusion of chronic pancreatitis and the inclusion of Midwestern states with a high prevalence of alcohol use [55]. Some countries do not have alcohol-induced AP due to cultural differences and prohibitions [27]. The onset of alcohol-induced AP in the general population usually occurs in the fourth decade. The average alcohol consumption in patients who develop AP is 150 g/day for 10–15 years before the initial presentation. Alcohol-induced AP is more commonly diagnosed during pregnancy probably because pregnant patients seek medical attention more commonly than female drinkers in the general population. Again, one must be cautious with the accusation of alcohol use as a cause due to its interrelation with hyperlipidemia.

#### 17.2.4.1 Pancreatic Pseudocysts

Most pregnant patients with pancreatic pseudocysts are nulliparous (84%), and the majority

(61%) manifest in the third trimester. While some claim that pancreatic pseudocysts are most frequently associated with alcohol-induced AP in pregnant and nonpregnant patients, current data show that hyperlipidemia is the most common cause (Table 17.6). A significant past medical history of alcohol misuse, AP, or both was elucidated in 38% [56]. Although 69% had no identifiable medical history, approximately a third had an undiagnosed predisposing factor—either familial hyperlipidemia or gallstones [56].

Non-gallstone AP in pregnancy is significantly more prone to pseudocyst formation [13, 25, 35, 57–60].

### 17.2.5 Primary Hyperparathyroidism

In the general population, PHPT is common, with its greatest frequency in postmenopausal women, up to 2–3% [61]. The incidence in women of childbearing age ( $<40$  years) is approximately 8/100,000 per year [62]. Approximately 0.5–1.4% of all PHPT occurs during pregnancy [63–65]. The most frequent cause of PHPT in the general population is a single parathyroid adenoma (85%), followed by parathyroid hyperplasia (15–20%) and, very rarely (less than 1%), by carcinoma [66, 67]. Hunter and Turnbull described the first case of PHPT during pregnancy in 1931 [68]. More than 100 cases have been reported in the English literature between 1931 and 1990 [62] and less than 200 until 2015 [69–74]. Parathyroid adenomas, as in the non-pregnant population, are the most common cause of PHPT during pregnancy (81.2%) [75]. At least three different causes may explain the relative paucity of data: (1) The average age of the initial manifestation of this disorder is higher than that

of women of childbearing age [61, 66, 67]; (2) about 80% of nonpregnant individuals with PHPT are characterized by an asymptomatic course of this disease [69]; and (3) some symptoms of PHPT may be misinterpreted as a simple consequence of pregnancy or other gestation-related disorders, while physiological changes during gestation may mask some abnormalities typical to PHPT [73, 76].

There is a 28-fold increased risk of AP in PHPT patients compared to the general population [77]. Whereas some series have suggested an association between PHPT and AP, community-based studies showed no increase in the incidence of AP among patients with PHPT compared with matched controls [72, 78]. PHPT is a rare etiology of hypercalcemic-induced AP, causing 0.4–2% of cases in the general population and significantly higher 7–13% during pregnancy [27, 63, 69–72, 79]. Others found a wide range of incidences of PHPT-induced AP in the general population of 1–12% [72, 80–82].

The simultaneous occurrence of PHPT and AP in pregnancy has only been reported 13 times until 1998 [70, 83–91]. There were no cases during the first trimester, and >90% had thyroid adenoma (89%) and only one thyroid carcinoma. There is an increased incidence of cholelithiasis in the general population with PHPT [92]. Therefore, the question is the real cause of AP during pregnancy in some PHPT cases.

### 17.2.6 Preeclampsia/Eclampsia

Between 1956 and 2007, 15 cases of AP were thought to be associated with preeclampsia [93].

### 17.2.7 Pancreatic Neoplasms

Pancreatic neoplasms, both benign and malignant, are uncommon during pregnancy. The most common are cystic pancreatic lesions, with 13 published cases diagnosed during pregnancy [94–98]. The first report was in 1968 by Smithers et al. [95]. In the general population, pancreatic mucinous cystic neoplasms occur almost exclusively in females. Only 11 cases of pancreatic adenocarcinoma [99] and 3 pancreatic neuroendocrine tumors were reported. Pancreatic cancer manifested as AP in a single case [99] with pancreatic adenocarcinoma.

### 17.2.8 Acute Fatty Liver of Pregnancy

For the description of acute fatty liver of pregnancy (AFLP), see Sect. 16.2.4.2. Approximately 15% of AFLP patients develop postpartum AP [100], which could be attributable to pancreatic ischemia [100].

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## 17.3 Etiopathogenesis

### 17.3.1 Introduction

Mnemonics for etiology of AP is “IT GET SMASHED”: **I**diopathic, **T**rauma, **G**allstones, **E**thanol, **T**umor, **S**teroids, **M**umps, **A**utoimmune, **S**corpion venom, **H**yperlipidemia, **E**RCP, **D**rugs. A comprehensive list of causes in the general population also applies to the pregnant population, with slightly different incidences (Table 17.1).

**Table 17.1** Causes of acute pancreatitis

|                                                                                                                                                                                                                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alcohol or methanol abuse (>100 g/day for >3 to 5 years)                                                                                                                                                            |
| Autoimmune diseases                                                                                                                                                                                                 |
| Choledochal cyst                                                                                                                                                                                                    |
| Cystic fibrosis                                                                                                                                                                                                     |
| Gallstones                                                                                                                                                                                                          |
| Hereditary (familial) pancreatitis (including a mutation of the cationic trypsinogen gene)                                                                                                                          |
| Hyperlipidemia or hypertriglyceridemia (1000 mg/dL)                                                                                                                                                                 |
| Hypercalcemia/hyperparathyroidism                                                                                                                                                                                   |
| Infection (coxsackie B virus, cytomegalovirus, mumps)                                                                                                                                                               |
| Ischemia from hypotension or atheroembolism                                                                                                                                                                         |
| Medications (ACE inhibitors, asparaginase, azathioprine, oral estrogens, antibiotics, 2', 3'-dideoxyinosine, furosemide, 6-mercaptopurine, pentamidine, sulfa drugs, valproate, thiazide diuretic, corticosteroids) |
| Neoplasm                                                                                                                                                                                                            |
| Pancreatic or periampullary cancer                                                                                                                                                                                  |
| Pancreas divisum                                                                                                                                                                                                    |
| Peptic ulcers                                                                                                                                                                                                       |
| Preeclampsia/eclampsia                                                                                                                                                                                              |
| Post-ERCP                                                                                                                                                                                                           |
| Postoperative inflammation                                                                                                                                                                                          |
| Post-renal transplant                                                                                                                                                                                               |
| Sphincter of Oddi stenosis                                                                                                                                                                                          |
| Blunt or penetrating trauma                                                                                                                                                                                         |
| Surgery (ischemia/perfusion/mechanical)                                                                                                                                                                             |
| Tropical pancreatitis                                                                                                                                                                                               |
| Vasculitis                                                                                                                                                                                                          |
| Viral infections                                                                                                                                                                                                    |
| Idiopathic                                                                                                                                                                                                          |

Elevation of intra-abdominal pressure leading to high pancreatic ductal pressure [101] and increased tonus of Oddi's sphincter may be other possible mechanisms to induce or promote AP of any cause.

The trigger events or precipitating factors for AP in 60% of pregnant women are associated with an excess high-fat/high-protein diet. The

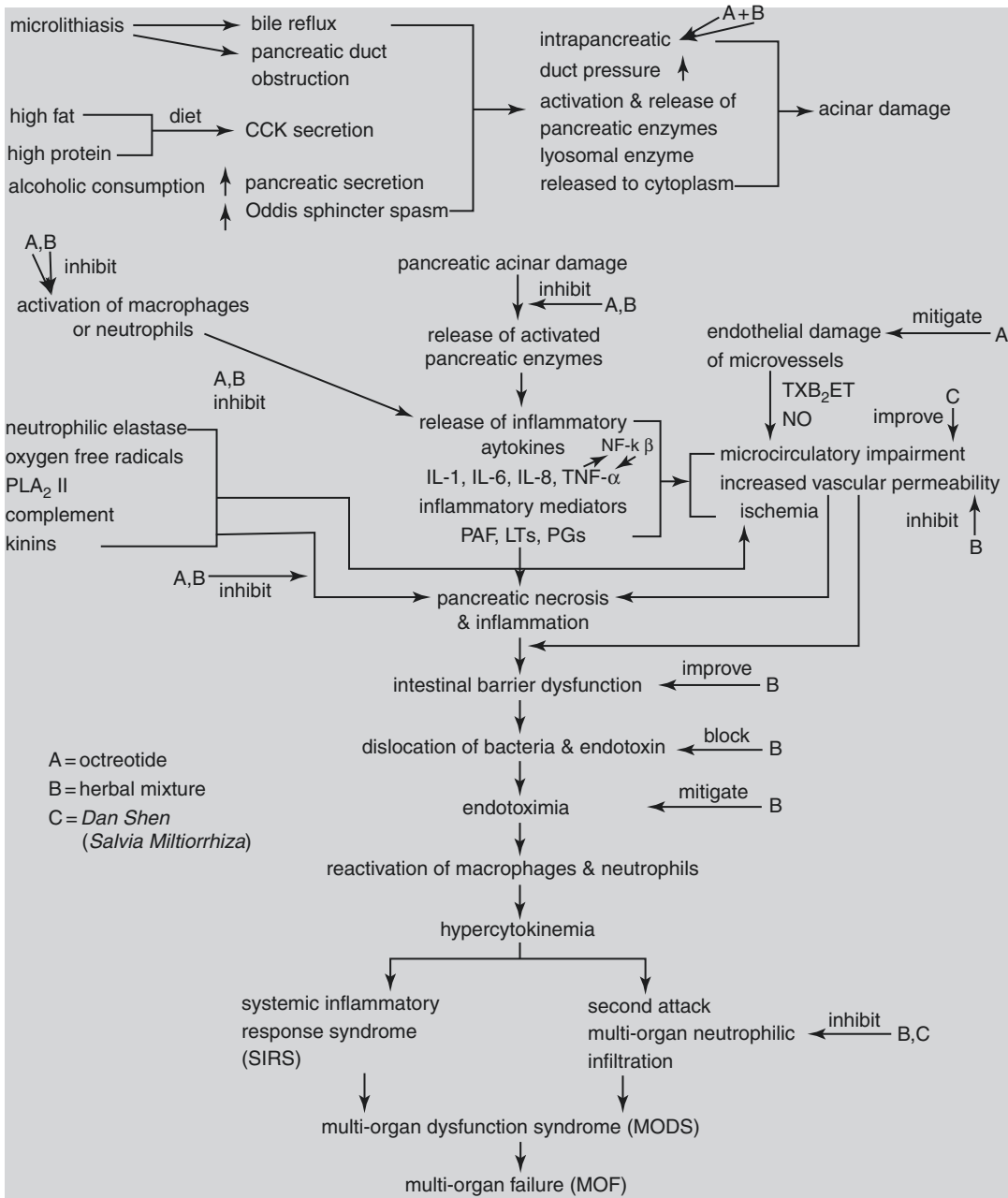
avored explanation may be that large amounts of bile/trypsin release can overwhelm the defense mechanism and activate other enzymes, resulting in local and systemic complications [102].

An additional factor in pregnancy is GDM. Severe diabetic ketoacidosis and hyperglycemia with associated dehydration could trigger AP in pregnancy. DM is a part of a metabolic syndrome (see Sect. 17.3.5). Idiopathic AP is diagnosed in 10% of cases [24], with a declining incidence as the knowledge of genetic causes, exogenous etiologies, and more precise diagnostic imaging accumulate.

**17.3.2 Biliary**

During pregnancy, gallstones and biliary sludge are accused as the most common causes of AP, causing pancreatic duct/ampulla of Vater obstruction with pancreatic hyperstimulation that increases pancreatic duct pressure, trypsin reflux, and activation of trypsin in the pancreatic acinar cells. The enzyme activation within the pancreas causes autodigestion, followed by local inflammation (Fig. 3.2). Pregnancy does not primarily predispose the pregnant woman to AP, but it does increase the risk of cholelithiasis and biliary sludge formation (see Chap. 16) [13]. Biliary AP occurs several years later (28.2 years) than non-biliary AP (24.4 years). In both groups, pregnant women were usually multiparous, and AP was mainly in the third trimester [24]. Global differences in the distribution of etiologies of AP exist (see Sect. 17.2), with a tendency for higher incidence during pregnancy than postpartum (Fig. 17.2) [103].





**Fig. 17.2** Schematic representation of step-by-step pathogenesis of (biliary) acute pancreatitis with the possible action of medications. CCK cholecystokinin, NO nitric oxide, TXB<sub>2</sub> thromboxane B<sub>2</sub>, TNF- $\alpha$  tumor necrosis factor  $\alpha$ , PAF platelet-activating factor, PG prostaglandin

17.3.3 Primary Hyperparathyroidism

17.3.3.1 Calcium-PTH Metabolism in Pregnancy

Pregnancy and lactation are characterized by alterations in calcium-PTH homeostasis, resulting from pregnancy-induced changes in the synthesis, metabolism, and excretion of calcium and calcitropic hormones [73, 104]. Early reports described *physiological hyperparathyroidism of pregnancy* with an increase in serum PTH levels beginning in the second trimester [105]. However, developing more accurate and specific methods has discredited this by showing a reduction, rather than an elevation, of intact PTH levels [106]. Mean serum PTH levels in nonpregnant women are 72% higher than in pregnant women [107]. These changes in PTH during pregnancy may be a response to altered calcium metabolism. Intravascular fluid expansion and hypoalbuminemia (albumin falls by 20%) make less protein available to bind calcium, thus lowering total (maternal serum calcium falls by 10%) but not ionized calcium [107]. Approximately 50% of serum calcium is protein-bound, primarily albumin; 10% is complexed to anions, and 40% circulates free as ionized calcium. In addition, increased urinary excretion of calcium occurs due to an increased glomerular filtration rate, and maternal serum calcium is actively transported across the placenta to the growing fetus [108]. Hypercalcemia is a (corrected) total serum calcium above the standard laboratory reference range (2.2–2.6 mmol/L). In pregnancy, the reference range is marginally lower depending on the trimester (Table 17.2).

The latter imposes an increased calcium requirement partly fulfilled by mobilizing calcium from the maternal skeleton. Together, these effects tend to lower maternal calcium levels [109]. During pregnancy, the placenta actively transports calcium ions to the fetus but does not allow the transfer of PTH [110]. Fetal blood, as

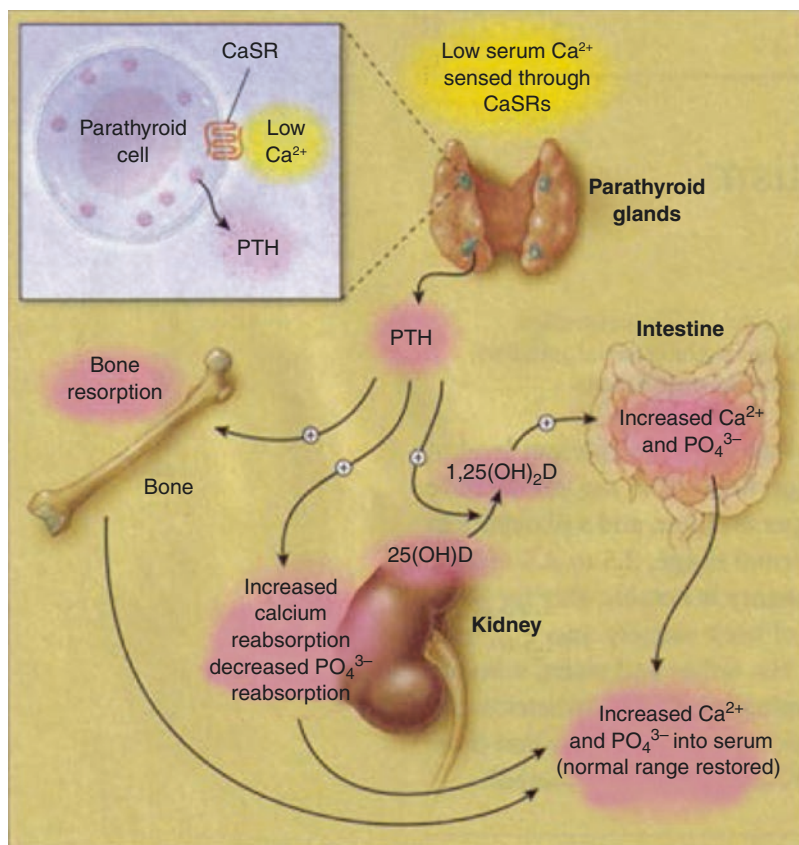
measured by cordocentesis, has a 0.5–1 mEq/L higher calcium concentration. Elevated concentrations are required secondary to increased fetal demand for adequate bone mineralization. Increased demand is met through active transport by the placenta via a maternal–fetal gradient of 1:1.4 [111, 112]. The parathyroid glands, which produce PTH, are stimulated by hypocalcemia and suppressed by high concentrations of calcium, magnesium, 1,25(OH)<sub>2</sub>D<sub>3</sub>, and hypomagnesemia. PTH influences calcium metabolism by directly reabsorbing bone and stimulating 1,25(OH)<sub>2</sub>D<sub>3</sub> formation. Maternal serum PTH levels, when measured by a sensitive assay that accurately measures the levels of intact PTH, are slightly decreased in the first half of pregnancy (20% of the mean nonpregnant values) and return to normal by mid-gestation [73]. Blood levels of 1,25(OH)<sub>2</sub>D<sub>3</sub> (calcitriol) increase early in gestation from stimulation of renal 1- $\alpha$ -hydroxylase activity by estrogen, placental lactogen, PTH, and placental synthesis of calcitriol [113]. Both free and total 1,25(OH)<sub>2</sub>D<sub>3</sub> increase in pregnancy because of an increase in vitamin D-binding protein (Fig. 17.3).

Elevated calcium levels ultimately result in fetal PTH suppression. Maternal PHPT can result in fetal hypercalcemia, increasing the risk of spontaneous abortion [115]. Maternal PHPT further suppresses fetal PTH, which accounts for the hypocalcemic effects on the fetus at birth [112]. However, they are more than offset by a large increase in intestinal calcium absorption during pregnancy [116]. Hormonal changes during pregnancy may also be responsible for an increase in the production or activity of the enzyme 1- $\alpha$ -hydroxylase in the kidney [117], which in turn may account for the observed differences between pregnant and nonpregnant women, including the elevation of 1,25-dihydroxyvitamin D [106], the slight increase in serum calcium levels [118], and the reduction in PTH levels [107]. Fetal 1,25-dihydroxyvitamin D, synthesized in

Table 17.2 Corrected serum calcium in pregnancy

| Normal           | 1st trimester    | 2nd trimester    | 3rd trimester    |
|------------------|------------------|------------------|------------------|
| 2.20–2.60 mmol/L | 2.25–2.57 mmol/L | 2.30–2.50 mmol/L | 2.30–2.59 mmol/L |

**Fig. 17.3** Control of mineral metabolism by parathyroid hormone; serum ionized calcium ( $\text{Ca}^{2+}$ ), parathyroid hormone (PTH), 1,25-dihydroxyvitamin D ( $1,25(\text{OH})_2\text{D}$ ), calcium-sensing receptors (CaSRs), phosphorus ( $\text{PO}_4^{3-}$ ), 25-hydroxyvitamin D ( $25(\text{OH})\text{D}$ ) [114]



the fetal kidney and placenta, acts as the major stimulus and regulator of calcium transfer across the placenta. It increases maternal gastrointestinal absorption of calcium by 150–400 mg/day; additionally, maternal urinary excretion is increased from 90 to 300 mg/day. Significant fetal calcium demands of 25–30 g are required in the third trimester for skeletal tissue mineralization. This requires active calcium transport across the placenta, and the fetal serum calcium remains higher than maternal blood. Conversely, neonatal hypocalcemia becomes an issue after delivery when the maternal transplacental supply of calcium ceases. This may occur because the neonate cannot mobilize calcium stores adequately because of prolonged parathyroid gland suppression.

The initiation and growth of kidney calculi may be attributed to the overlapping of increased calcium load, secondary to enhanced PTH synthesis and release, and a pregnancy-induced increase in urine calcium excretion.

### 17.3.3.2 Calcium-Induced Acute Pancreatitis

After eliminating other causes, mean plasma calcium level seems to be the only predictive factor for AP [77, 80, 119]. In addition, genetic mutations constitute a more significant risk factor for AP than serum calcium [82].

The pathophysiologic mechanism that leads to AP seems more related to hypercalcemia than PHPT. Hypercalcemia from any cause can lead to AP.

Calcium ions cause calculus deposition within the pancreatic ductules, with consequent obstruction and inflammation [120]. Moreover, calcium can trigger the AP cascade by promoting the conversion of trypsinogen to trypsin [121]. The interrelation between AP and parathyroid function can

be summarized: (1) AP has a tendency to hypocalcemia and secondary hyperparathyroidism [122, 123]. Compensation need is correlated to AP severity as shown by PTH level [124]; (2) SAP can lead to overt hypocalcemia through relative deficiency in PTH secretion [123] because exogenous administration of PTH normalizes calcium level [125]; (3) in SAP, resistance to PTH action in bones and kidneys may occur because of fluid sequestration and reduction in efficient arterial blood volume [122]; and (4) once the diagnosis of PHPT-induced AP is established, parathyroidectomy is mandatory preventing its recurrence [63, 80].

AP developed in 3/4 pregnancies complicated by PHPT, while never before and between pregnancies. Therefore, gestation makes PHPT patients prone to AP. AP occurs more frequently in primipara, mainly in the first and third trimesters [74, 75]. PHPT can result in calcifications in the pancreatic ducts, thereby blocking secretions, damaging the pancreatic tissues, and resulting in AP [83]. Usually, this is present with higher calcium levels than PHPT without AP [83]. Although the absolute calcium level is a significant predictor, it may attenuate during pregnancy, and individual predisposing factors may be necessary to manifest pancreatic inflammation [91].

Although most young women with hypercalcemia have PHPT, other unusual causes should be ruled out (Table 17.3).

**Table 17.3** Causes of hypercalcemia during pregnancy other than primary hyperparathyroidism

|                                                |
|------------------------------------------------|
| Familial hypocalciuric hypercalcemia           |
| Postpartum hypercalcemia in hypoparathyroidism |
| PTHrP-induced hypercalcemia                    |
| Malignancy                                     |
| Thyrotoxicosis                                 |
| Adrenal insufficiency                          |
| Vitamin D overdose                             |
| Vitamin A overdose                             |
| Thiazide diuretics                             |
| Lithium                                        |
| Granulomatous disease                          |
| Sarcoidosis                                    |
| Tuberculosis                                   |
| Histoplasmosis                                 |
| Coccidioidomycosis                             |
| Milk-alkali syndrome                           |
| Acute/chronic renal failure                    |
| Total parenteral nutrition                     |

### 17.3.4 Acute Fatty Liver of Pregnancy

See Sect. 16.2.4.2. Approximately 34% of the general population who died from AP had macroscopic liver steatosis [126]. Therefore, hepatic problems could be the origin of pancreatic disease by observing extraordinarily high concentrations of lipoperoxide in the bile of patients with pancreatic disease [127]. Pancreatic toxicity is probably due to FFAs, similar to HTG-induced AP (see Sect. 17.3.5). The hypothesis is that the accumulation of long-chain metabolites of 3-hydroxyacyl is toxic to the liver and pancreas [128]. In addition to its toxic effects, AP from AFLP could be attributable to pancreatic ischemia [100].

### 17.3.5 Hyperlipidemia/Dyslipidemia

Early pregnancy is an anabolic phase characterized by increased hepatic triglyceride production and enhanced triglyceride removal from circulation, resulting in increased fat deposition in maternal adipose tissue. In contrast, late pregnancy is a catabolic phase with the release of FFAs from adipocytes enhanced by relative insulin resistance and stimulating hormone-sensitive lipase by placental hormones. These metabolic changes allow the metabolism during pregnancy to store energy in early pregnancy to meet the energy requirements of late gestation.

Maternal hypertriglyceridemia and hypercholesterolemia (*maternal physiologic hyperlipidemia*) contribute to fetal growth and development and serve as an energy depot for maternal dietary TGs and fatty acids [129], sparing the glucose for the fetus. During pregnancy, serum lipid and lipoprotein concentrations are modulated by complex interactions between genetic and metabolic factors. The *estrogen:progesterone ratio* is essential in balancing lipoprotein metabolism during pregnancy. Progesterone opposes the action of estrogen on lipoprotein metabolism [130]. During the first trimester, the ratio is low, indicating a predominantly progesterone-mediated effect on lipid metabolism with lipoprotein levels lower than prepregnancy baseline levels. The total cholesterol and TG increase dur-

ing the second and third trimesters due to increased estrogen levels leading to an increase in lipoprotein levels (Fig. 17.4).

Plasma TG levels increase two to three times [132], rarely exceeding 3.3 mmol/L (300 mg/dL). This physiological increase during pregnancy is not sufficient to cause AP. Preexisting genetic abnormalities in lipid metabolism may be exacerbated during pregnancy and can cause gestational hyperlipidemic AP. The elevation in TG levels is greater than that of cholesterol (an increase of 50%) and phospholipids (Fig. 17.4).

Lipoprotein lipase (LPL) is a crucial enzyme for the hydrolysis of TG from chylomicrons and VLDL particles of blood plasma. Exogenous and endogenous mechanisms can modulate LPL activity. Exogenous mechanisms include a combination of (1) a human placental lactogen-related increase (secreted by trophoblast cells) and prolactin level increase inhibit adipose tissue LPL activity resulting in a rise in the concentration of plasma TG and FFA level in serum [133], (2) hepatic synthesis of VLDL results in increased production of TG-rich lipoproteins [134], and (3) up- or downregulation by insulin, estrogen, and medications [135, 136].

During pregnancy fasting, plasma TG levels increase predominantly through the increased liver synthesis of TG and VLDL in response to elevated estrogen levels [137]. The presence of

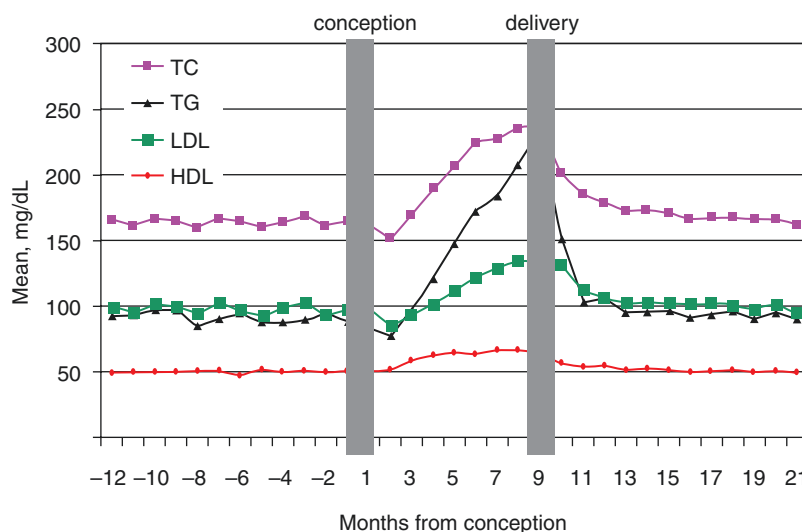
lipoprotein receptors in the placenta, along with LPL and intracellular lipase activities, allows the release of FFAs to the fetus [132]. Endogenous mechanisms consist of the LPL gene mutations. More than 30 mutations have been identified in the LPL gene in women with gestational AP [138, 139], the first in 1994 [138].

Mutations of the LPL gene (Fig. 17.5) may result in partial or, rarely, complete LPL deficiency. Complete deficiency usually but not invariably presents in childhood with hyperchylomicronemia, eruptive xanthomatosis, and recurrent AP. It could be responsible for a tenfold increase in plasma TG levels [139]. The assumption is that the rarity of the syndrome of hyperlipidemia and AP in pregnancy in patients with this specific genetic defect may be due to the undetected additional mutation in affected patients [140].

Additionally, the clearance of VLDL and chylomicrons decreases due to a reduction in LPL at the capillary endothelium [135, 141]. This appears to be due to a decrease in LPL synthesis in adipose tissue and possibly skeletal muscle through the downregulation of LPL gene expression by estrogen [135].

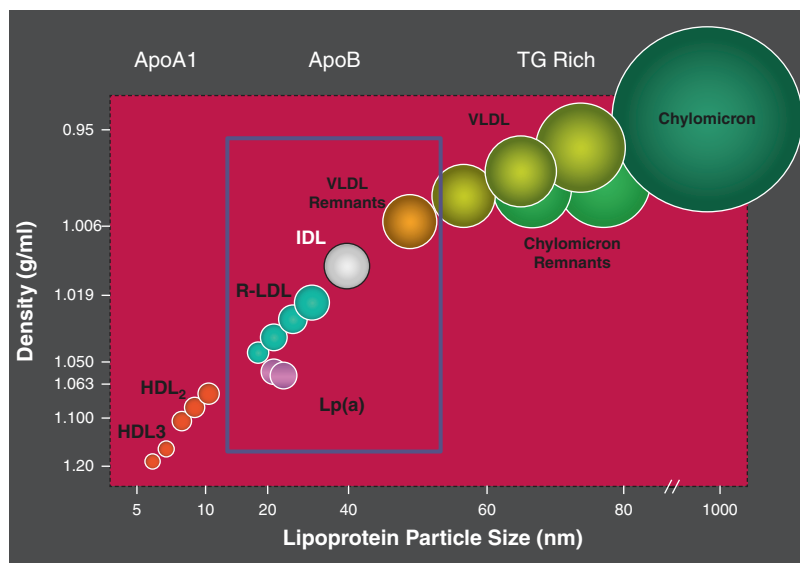
Compared to hypercholesterolemia and mixed hyperlipidemia, HTG increases the risks of hyperlipidemic AP in pregnancy [142]. The precise mechanisms for the pathogenesis of HTG-

**Fig. 17.4** Lipid level variations during normal pregnancy are characterized by an initial decrease from the prepregnancy baseline levels during the first trimester, followed by a gradual increase and peaking before the delivery. (Reproduced with permission from [131])





**Fig. 17.5** Lipoprotein size–density relationship. Lipid subclasses are present in a continuum of size and density, with a substantial gradient for the TG-rich lipoproteins IDL, VLDL, and chylomicrons. (Figure courtesy of Atherotech Labs, Inc., Birmingham, AL)



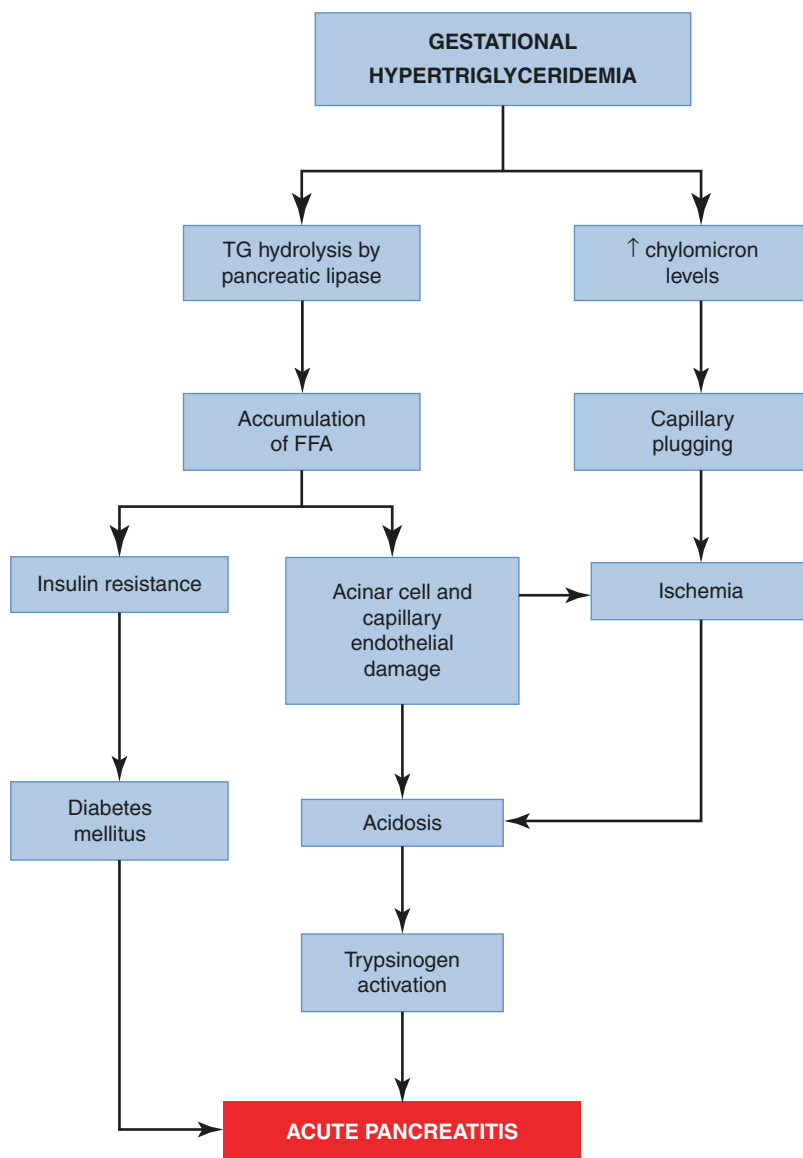
induced AP are not established. HTG is 5× more common in pregnant women with AP (38%) than in pregnant women without AP (9%) [143]. Hydrolysis of excessive TG-rich lipoproteins by high levels of pancreatic lipase releases very high concentrations of FFAs, which exceed the binding capacity of plasma albumin, thus resulting in self-aggregating FFA micellar structures with detergent properties [144]. The elevated circulating FFAs impair endothelium-dependent vasodilation [145], and the decreased endothelial function may depend on enhanced oxidative stress [146]. Inflammatory effects of TG-rich lipoproteins result from increased expression of leukocyte adhesion molecules and monocyte adherence on endothelial cells in response to the inflammatory cytokine tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) [147]. Aside from producing an alteration in plasma TG concentrations, estrogen could have toxic effects on the pancreas. Pancreatic acinar cells have significant amounts of an estradiol-binding protein [148]. Estrogen increases LDL receptors [149] and could promote lipid uptake into acinar cells. Sufficient excess lipid uptake leads to lipotoxicity and cellular apoptosis, which is best characterized in muscle cells [150]. The observation supports the direct effects of estrogens on the pancreatic function that pancreatic amylase release in the rat is stimulated by estro-

gen [151]. On the other hand, an elevation in estrogen may increase the synthesis of TG and depress plasma postheparin lipolytic activities (PHLA), lowering the removal efficiency of TG during pregnancy. The production rates of TG and total cholesterol at the end of pregnancy are markedly increased to 140% and 50%, respectively, compared to the nonpregnant period [152]. Additionally, TGs universally increase during an episode of AP. Whether the elevated TGs are an epiphenomenon of the AP or the actual cause of the inflammation can be challenging to differentiate. Mild-to-moderate elevations of TGs are seen in up to 50% of all-cause AP and are generally regarded as an epiphenomenon rather than a cause. However, the increase caused by AP alone is transient, peaking at 72 h and declining to near normal values in 2 weeks [50].

The FFA micelles injure the vascular endothelium and acinar cells of the pancreas, producing a self-perpetuating ischemic/acidic environment. In this acidic environment, FFAs activate trypsinogen and trigger acute edematous and necrotizing AP. Another theory favors ischemia secondary to plasma hyperviscosity due to severe chylomicronemia [153]. However, these two theories are not mutually exclusive (Fig. 17.6). Additionally, physical damage by cholesterol crystals might cause microvascular endothelial cell disruption [144].

**Fig. 17.6**

Pathophysiology of HTG-induced acute pancreatitis. *TG* triglyceride, *FFA* free fatty acid. (Modified from [154] under the CC Attribution License)



The development of marked HTG, specifically in pregnancy, in the absence of DM, drug, or alcohol intake, raises the possibility of partial defects in TG metabolism (Table 17.4).

HTG-induced AP occurs when TG levels are over 1000 mg/dL, while recently, it has been claimed that most AP cases occur when levels exceed 3000 mg/dL [156].

Patients with severe HTG should be evaluated for a genetic disorder in lipid metabolism. According to Fredrickson's classification of dyslipidemias, types I, IV, and V are associated with severe HTG and predispose to AP [157]. Types I and V can present with AP without an exacerbating factor. In contrast, type IV usually requires secondary precipitating factors (e.g., poorly controlled DM, alcohol use, estrogen, pregnancy, or medications that can increase or raise TG levels) [45]. Type I (familial chylomicronemia) often

**Table 17.4** Acquired/secondary causes of hypertriglyceridemia

|                                                                                                                                                                                                                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alcohol excess                                                                                                                                                                                                                                     |
| High-carbohydrate diet                                                                                                                                                                                                                             |
| Insulin resistance                                                                                                                                                                                                                                 |
| Obesity                                                                                                                                                                                                                                            |
| Type 2 diabetes mellitus                                                                                                                                                                                                                           |
| Pregnancy                                                                                                                                                                                                                                          |
| Chronic renal failure, nephrotic syndrome                                                                                                                                                                                                          |
| Hypothyroidism                                                                                                                                                                                                                                     |
| Cushing syndrome                                                                                                                                                                                                                                   |
| Acute pancreatitis                                                                                                                                                                                                                                 |
| Viral hepatitis                                                                                                                                                                                                                                    |
| Biliary obstruction/cholestasis/biliary cirrhosis                                                                                                                                                                                                  |
| Multiple myeloma, monoclonal gammopathy                                                                                                                                                                                                            |
| Glycogen storage disease                                                                                                                                                                                                                           |
| Lipodystrophy                                                                                                                                                                                                                                      |
| Systemic lupus erythematosus                                                                                                                                                                                                                       |
| Nephrotic syndrome                                                                                                                                                                                                                                 |
| Chronic renal failure, uremia                                                                                                                                                                                                                      |
| Stress                                                                                                                                                                                                                                             |
| Sepsis                                                                                                                                                                                                                                             |
| Ileal bypass surgery                                                                                                                                                                                                                               |
| Drugs—exogenous estrogens, tamoxifen, glucocorticoids, $\beta$ -blockers, amiodarone, thiazide diuretics, cyclosporine, retinoids, bile acid-binding resins, antiretrovirals (protease inhibitors), propofol, clozapine, parenteral lipid infusion |

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presents in infancy and is caused by an autosomal recessive trait resulting in LPL or apo C-II deficiency. Type IV (familial HTG or familial combined hyperlipidemia) is autosomal dominant and presents in adulthood.

In addition to HTG-induced AP, hyperlipidemia is an attendant risk for cholesterol gallstones and intrahepatic cholestasis of pregnancy [158].

### 17.3.6 Hypothyroidism

Hypothyroidism has been documented as a cause of HTG and HTG-induced AP [42, 159]. In the general population, hypothyroidism is present in 1.4–13% of patients with hyperlipidemia [160]. Guidelines from the *American Association of Clinical Endocrinologists* and the *American Thyroid Association* recommend screening for hypothyroidism in newly diagnosed hyperlipid-

emia before starting a lipid-lowering agent [161, 162]. Low circulating free thyroid hormone levels may impair adipose tissue LPL activity, raising LDL levels.

### 17.3.7 Alcohol Abuse

The role of alcohol in the etiopathogenesis and occurrence of AP is complex. However, increased oxidative stress [163], disruption of cytosolic calcium homeostasis [164], and changes in gene expression [165] in the pancreas seem to be involved. Nevertheless, only up to 5% of heavy alcohol drinkers (4–5 drinks/day) develop AP after 10–20 years [166]. A potential role for the type of beverage results from a decline in the incidence of AP alongside a decline in the sales of spirits, despite increased sales of beer and wine [167]. The ethanol metabolism induces oxidative stress, which depletes cellular glutathione storage and results in lipid peroxidation and damage to pancreatic tissue [163]. However, ethanol alone is not enough to induce AP [168]. Beer [169] and wine [169] include polyphenols with antioxidant capabilities. Other constituents in spirits, such as long-chain alcohols, are more potent than ethanol in inducing oxidative stress [169]. Spirits deplete antioxidant capacities more readily than beer or wine [169]. Thus, other constituents in spirits might induce AP in combination with ethanol or alone. Those drinking spirits might also have lower reserves of antioxidants at baseline, which could be depleted rapidly after intake of spirits. Alcohol use is associated with an increased risk of AP in a dose-dependent manner [170] but consumed alcoholic beverages contain other constituents that are a potential cause of injury to the pancreas. Also, the patterns of drinking indicate that the more harmful the pattern of drinking (i.e., the more heavy drinking), the higher the rates of alcohol-induced AP [171], with a threshold of approximately four drinks daily [172].

The theory from 1955 was that increased intra-abdominal pressure is the crucial event in developing AP of any cause. It may be that the chronic alcoholic may hiccup, inducing a pancreatic attack by fixing his diaphragm and sending

his bile juice up the pancreatic duct [7]. The constant increase in intra-abdominal pressure, especially in late pregnancy, could contribute to the risk of AP.

### 17.3.8 Medications

AP in the general population due to medications is unusual, although the incidence may be increasing, with the incidence of 0.3–1.4% in the general population [173, 174]. Over 55 medications have been implicated, and the list continues to grow. Drug-induced AP in pregnancy is extremely rare [13]. Proposed criteria for classifying drugs as having an association with AP are [175] as follows:

- AP develops during treatment with the drug,
- Other likely causes of AP are not present,
- AP resolves upon discontinuing the drug,
- AP usually recurs upon readministration of the drug.

Assignment to a particular category (definite, probable, or possible association) is often arbitrary due to inadequate and conflicting data and interpretation bias. The pathogenesis of drug-induced AP may be due to an *allergic response* (6-mercaptopurine, aminosalicylates, and sulfonamides), a direct *toxic effect* (diuretics, sulfonamides, and steroids), or an *indirect effect* (codeine causes rapid but transient spasm of the sphincter of Oddi, some medications cause TG elevation). Medications associated with elevated TG that can cause AP through the hypertriglyceridemia pathway include protease inhibitors, propofol, olanzapine, mirtazapine, and isotretinoin (Table 17.4).

Estrogen therapy in DM may lead to an extreme HTG, particularly in an uncontrolled glycemic state, and possibly induce AP [41, 176, 177]. In type I DM, the absence of insulin

reduces the ability of LPL to reduce TG into FFA, resulting in elevated TG levels [178]. In type II DM, insulin resistance leads to enhanced production and reduced clearance of TG [179]. The role of alcohol in HTG is unclear but may be attributed to alcohol competing with FFAs for oxidation, leaving more FFAs available for TG synthesis [45]. Some authors claim that alcohol alone does not cause HTG but more likely exacerbates underlying genetic hyperlipidemia [176]. Accordingly, hormone therapy in women is not recommended when TG is >500 mg/dL due to a heightened risk of HTG AP [180]. Exogenous estrogens (especially in high levels during assisted reproduction) elevate TGs by increasing the production of TG-carrying VLDLs by the liver and reducing the levels of LPL and hepatic lipase, thus reducing TG clearance while also elevating TGs by augmentation of insulin resistance [177]. There are six reported cases of IVF-induced HTG with secondary AP [181]. The pathophysiology of IVF-induced hypertriglyceridemia is likely related to estrogen therapy.

Tamoxifen causes a small but significant decrease in high-density lipoprotein (HDL) cholesterol, unlike estrogen, which elevates HDL. In women with HTG, tamoxifen's ability to increase the TG level is especially pronounced, to the extent that it may induce AP [177]. Clomiphene citrate is a synthetic estrogen analog with a biochemical structure similar to tamoxifen. Clomiphene elevates the TG level, mainly in women with a predisposed risk for HTG due to mutations in enzymes such as LPL [182]. Apoprotein E (apo E), particularly apo E allele 2, has been associated with higher TG levels in pregnant patients with chylomicronemia [138].

Gemeprost is a synthetic prostaglandin E1 (PGE1) analog. PGE1 increases pancreatic and mesenteric blood flow [183] and protein production. For instance, PGE1 stimulated the production and secretion of  $\alpha$ -amylase from the porcine pancreas in vitro [184] and enzyme output in dogs in vivo [183]. These facts would point out that mifepristone or gemeprost are possible causative agents during a medical abortion [185]. Identifying a causative medication is a problem

because these patients often receive other medications, such as paracetamol or codeine.

Diuretics can induce AP [186, 187]. Preeclampsia-associated AP (see Sect. 17.3.11) is rare and is associated with microvascular abnormalities involving cerebral, placental, hepatic, renal, and splanchnic circulation. Pancreatic vasculature is also altered and prone to AP. In one study, 66.7% of preeclampsia-associated AP received diuretics [14]. AP associated with angiotensin-converting enzyme inhibitors reflects angioedema of the gland. It is unclear whether preeclampsia/eclampsia, diuretics, or its combination causes AP during pregnancy.

### 17.3.9 Post-ERCP

See Sect. 16.2.5.4.

### 17.3.10 Pancreatic Neoplasms

AP may be a complication of pancreatic cancer due to infiltration of the pancreas by the tumor or obstruction of enzyme flow from the pancreatic duct/ampulla. Symptomatic pancreatic tumors during pregnancy are most commonly mucinous cystic neoplasms. First, these are the largest space-occupying pancreatic tumors. Second, ovarian-like stroma exists exclusively in female patients with mucinous cystic neoplasms, often immunohistologically positive for progesterone or estrogen receptors. The physiological increase in the blood concentration of these hormones could promote this type of tumor [97, 188]. One of the possibilities is that mucinous cystic neoplasms originate from primitive ovarian cells, which are incorporated into the embryonic pancreas when the left primordial gonad is close to the dorsal pancreatic anlage during embryogenesis [189]. The dorsal pancreatic anlage gives rise to the body and tail of the pancreas, and this hypothesis could explain the predilection of these tumors for the distal pancreas. Another possibility is that the neoplastic epithelial cells of these tumors might induce ovarian stromal differentia-

tion in cells that typically reside in the pancreas. This concept is based on the fact that the stroma in the fetal pancreas is morphologically similar to that of mucinous cystic neoplasms [190].

Pancreatic mucinous cystic neoplasms present a clinical problem due to their malignant potential. Mucinous cystadenocarcinoma can arise de novo or can be an evolution of the benign form. Large tumor size is a predictive factor of malignant forms. It is difficult to conclude whether this increased growth during pregnancy increases the risk for malignant transformation [94]. It remains unclear whether high levels of estrogen and progesterone in pregnancy accelerate the malignant transformation of a benign tumor into a malignant tumor.

### 17.3.11 Preeclampsia/Eclampsia

The incidence of preeclampsia in patients with PHPT is 25% [75], especially with causative parathyroid adenoma [112, 191, 192]. Similarities in endothelial damage, insulin resistance, and cardiovascular disease shared between the PHPT and preeclampsia may support the hypothesis that a relationship exists between these two pathologic processes. In addition, maternal vitamin D deficiency has been associated with preeclampsia. This also supports the concept that mechanisms of calcium homeostasis affect blood pressure in pregnant patients with preeclampsia [192].

The association between pregnancy-induced hypertension and dyslipidemia has clinical importance. Metabolic syndrome in previous decades among women <20 years was 23.4%. These results, with the high incidence of overweight and obesity, suggest the susceptibility of women of reproductive age to hypertensive disorders of pregnancy. Pregnancy-induced hypertension is several fold higher in hyperlipidemic patients [193], and preeclampsia is preceded by raised serum triglyceride levels [194] in up to 50% [193]. Cholesterol levels were not statistically different between cases and controls in any form of hypertension levels [194]. In preeclampsia, decidual vessels show fibrinoid necrosis of



the vessel wall and focal accumulation of lipid-laden macrophages, similar to atherosclerosis, suggesting enhanced lipid peroxidation may be involved in the foam cell formation. Preeclampsia is associated with microvascular abnormalities/alterations [195] that may involve cerebral, placental, hepatic, renal, and splanchnic circulation. The pancreatic vasculature is likely altered and prone to AP, which often results in pancreatic necrosis [195]. It is difficult to conclude whether preeclampsia or diuretics cause AP due to the high incidence of diuretics for preeclampsia [14, 196] (see Sect. 17.3.8).

### 17.3.12 Puerperium

AP can occur during any trimester, mainly during the third and rarely in the puerperium [13]. Most AP resolves during medical or surgical therapy, but some are resolved only after CS when all the gestational state (primarily hormonal) changes to return to the pregestational state. Partly, it can be explained by lowered intra-abdominal or intra-pancreatic pressure after delivery. Biliary AP is most common in young postpartum women (see Sect. 16.1.3). Some patients eject small gallstones from the gallbladder during the postpartum period when gallbladder contraction is restored, and some of these women develop AP. In contrast, in older women with reduced gallbladder contractility, most gallstones likely remain in the gallbladder until dissolved by less lithogenic bile.

## 17.4 Clinical Presentation

AP presents in the same way during pregnancy as in the nonpregnant state. However, clinical diagnosis is challenging due to the similar presentations of many acute abdominal conditions and maternal changes during pregnancy.

### 17.4.1 Medical History

The family history of hyperlipidemias, DM, AP, pregnancy-induced hypertension, preeclampsia/eclampsia, gallstones, etc., should be noted.

These conditions should be corrected before or during pregnancy planning to eliminate or minimize the possibility of AP during pregnancy. Since there is no safe alcohol level during pregnancy, it should be banned. The T-ACE [Take (number of drinks), Annoyed, Cut down, Eye-opener] TWEAK (Tolerance, Worried, Eye-opener, Amnesia, Kut down), and AUDIT-C (AUDIT consumption) alcohol screening questionnaires are helpful in pregnant women. However, these have not yet been validated in the pregnant population [197].

The symptoms of AP in pregnancy could be nonspecific; the predominant symptom is upper abdominal pain. It is usually midepigastric and radiates to the back in 40% of the cases [13]. Pain is commonly accompanied by midepigastric tenderness, nausea, and vomiting [198]. Fever may be present [198]. Some cases may have persistent vomiting, abdominal distension, and tenderness in the whole abdomen. The duration of symptoms varies from 1 day to 3 weeks. In severe cases, sinus tachycardia, hyperventilation, and the smell of acetone in breath are present. Fever, unstable respiratory and circulatory function, shock, and gastrointestinal bleeding indicate SAP. Marcus, in 1930, emphasized that persistent vomiting in pregnancy could be related to AP and that blood and enzyme studies should be done [199].

#### 17.4.1.1 Primary Hyperparathyroidism

Asymptomatic PHPT in the general population is rare. Thorough anamnesis reveals subtle symptoms. The most frequent digestive manifestations are constipation, heartburn, nausea, and appetite loss in 33%, 30%, 24%, and 15%, respectively [200]. Unlike the general population, 4/5 of PHPT pregnant patients experience a clinically overt course [69, 74], most commonly with nephrolithiasis [69, 201]. Symptomatic PHPT is rarely detected in pregnancy due to the physiological changes that mask the symptoms—maternal blood volume expansion, hypoalbuminemia, increased fetal calcium requirements, and increased calcium clearance. Between 23 and 80% of PHPT patients are asymptomatic or unrecognized [73, 79, 104].

The following conditions raise suspicion: appropriate symptoms or signs (especially nephrolithiasis or AP), hyperemesis beyond the first trimester, history of recurrent spontaneous abortions/stillbirths, neonatal deaths, neonatal hypocalcemia, or tetany. Sometimes initial maternal presentation is due to complications, which include hyperemesis gravidarum, pre-eclampsia, tremors, fractures, depression, headache, blurred vision, uremia, seizures, and coma [64, 69, 75].

The most common indicator of PHPT during pregnancy is the development of neonatal tetany [64].

PHPT is a risk factor for eclampsia [75, 202], which can also be present during pregnancy and could mask PHPT.

#### 17.4.1.2 Acute Fatty Liver of Pregnancy

See Sect. 16.2.4.2.

The characteristic of AFLP is that abnormalities in renal dysfunction typically became evident after the abnormalities in liver dysfunction [203]. AP is typically noticed (radiographic and serum abnormalities) after hepatic and renal dysfunction [128, 203].

#### 17.4.1.3 Hypertriglyceridemia

Though the initial presentation of HTG-induced AP is similar to AP due to other etiologies, some features should lead to the consideration of HTG-induced AP. Poorly controlled DM, alcoholism, obesity, prior AP, and personal or family history of hyperlipidemia suggest HTG-induced AP [41, 45]. Alcoholism or DM has been reported in 72% of HTG-induced AP [41, 45].

#### 17.4.1.4 Medications

Drug-induced AP in the general population has no distinguishing clinical features. A high index of suspicion and careful drug history is essential for the diagnosis. The time course of developing the disorder depends upon the drug involved. AP may develop within a few weeks after beginning a drug associated with an immunologically mediated adverse reaction. In this setting, the patient may also have a rash and eosinophilia. In contrast, patients taking valproic acid, pentamidine, or didanosine may not develop AP until after many months of use, presumably due to the chronic accumulation of toxic metabolic products. Thus, patients restarted on their medications should be monitored, and the drug should be promptly discontinued if symptoms recur. Mothers or physicians discontinue many medications during pregnancy when not sure about teratogenicity.

#### 17.4.2 Physical Examination

Physical findings vary with the severity of illness; in moderate-to-severe AP, the patient appears acutely ill, lying in the “fetal position” with flexed knees, hips, and trunk. Abdominal tenderness is common, and muscle rigidity is present in diffuse peritonitis. Bowel sounds, secondary to paralytic ileus, are usually hypoactive or absent. SAP results in third-space fluid losses and systemic toxicity. Hypovolemia can lead to tachycardia up to 150/min and low blood pressure. Also, the temperature may increase because of the severe retroperitoneal inflammatory process. Dyspnea, tachypnea, and shallow respirations resulting in hypoxemia may be present.

Clinical signs are the same as in the non-pregnant population. *Cullen’s sign* (Fig. 9.3) and *Grey Turner’s sign* are rare but among the most common. *Fox’s sign* is ecchymosis of the upper thigh with a superior border, and *Stabler’s sign* is bruising of the groin. Differential diagnosis of the diseases coexistent with non-iatrogenic Cullen’s sign is presented in Table 9.2.

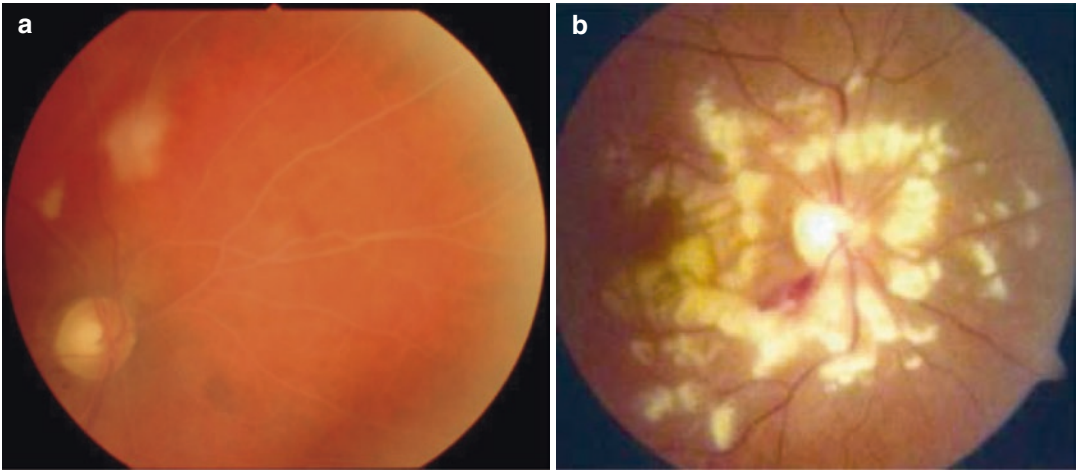
Some physical findings point to a specific cause of AP: jaundice in biliary origin, spider angiomas in alcoholic or xanthomata, and lipemia retinalis in hyperlipidemic AP. HTG can lead to chylomicronemia syndrome, with eruptive xanthomata over extensor surfaces of the arms, legs, buttocks, and back indicating triglyceride levels greater than 1000 mg/dL

(Fig. 17.7) [205, 206], lipemia retinalis (Fig. 17.8a), and hepatosplenomegaly from fatty infiltration of the liver [58, 204, 206]. Lipemia retinalis should be distinguished from Purtscher-like retinopathy (Fig. 17.8b) found with AP, pre-eclampsia, and childbirth (and other non-traumatic conditions). It is associated with a constellation of retinal findings, including cot-



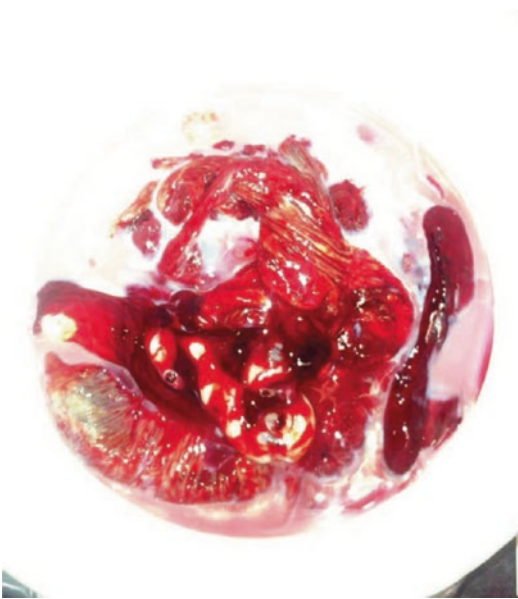
**Fig. 17.7** Clinical manifestations of hyperlipidemia. (a) Achilles tendon xanthoma (heterozygous familial hypercholesterolemia—type IIa); (b) tendon xanthomata on the dorsum of the hand (heterozygous familial hypercholesterolemia); (c) subperiosteal xanthomata (heterozygous familial hypercholesterolemia); (d) planar xanthoma in

antecubital fossa (homozygous familial hypercholesterolemia); (e) striate palmar xanthomata (type III); (f) tubero-eruptive xanthomata on the elbow and extensor surface of arm (type III); (g) milky plasma from severe hypertriglyceridemia; (h) eruptive xanthomata on the extensor surface of the forearm (severe hypertriglyceridemia) [204]



**Fig. 17.8** (a) Lipemia retinalis associated with hyperlipidemia. The rare and asymptomatic creamy white appearance of retinal vessels occurs when triglyceride value reaches more than 2000 mg/dL (22.6 mmol/L)—the effect due to dispersion of light caused by a high value of circulating chylomicrons in the blood, most commonly occur-

ring in familial hyperchylomicronemia. (Reproduced with permission from [207] under the CC BY 3.0). It should be distinguished from (b) Purtscher-like retinopathy found in acute pancreatitis and preeclampsia. (Reproduced with permission from [208] under the CC BY 3.0)



**Fig. 17.9** Placenta covered with milky fluid suggestive of severely increased serum lipid levels. (Reproduced with permission from [209] under the CC Attribution License)

The cause of the AP can be found during emergent exploration. Intraperitoneal fluid can be milky and lipemic. Similarly, emergent CS reveals a placenta covered with milky fluid (Fig. 17.9), contributing to the diagnosis of hyperlipidemic AP [209].

## 17.5 Diagnosis

With a clinical suspicion of AP, laboratory investigations, and imaging modalities are mandatory. Some important typical laboratory values in pregnant and nonpregnant women are compared in Table 17.5. Serum total calcium, PTH, and 25-hydroxyvitamin D values do not change during pregnancy, while 1,25-dihydroxyvitamin D and PTH-related protein levels increase [211]. Until 1951, most diagnoses were made during an operation or an autopsy. In only 5.7%, the diagnosis was made clinically [5]. Approximately 15% of pancreatic pseudocysts were diagnosed at emergency laparotomy [56]. With modern imaging techniques, all pancreatic pseudocysts are discovered before surgery.

ton-wool spots, retinal hemorrhages, optic disk edema, and *Purtscher flecken* (areas of inner retinal whitening).



**Table 17.5** Calculated upper (97.5 percentile) and lower (2.5 percentile) limits for the reference interval and 90% confidence intervals (in brackets) during different stages of pregnancies and postpartum. The samples denoted as pre-delivery were collected 0–14 days before delivery. Postpartum samples were collected at least 45 days after delivery

|                                                | Lower limit      | Upper limit      |
|------------------------------------------------|------------------|------------------|
| <b>Alanine aminotransferase (ALT) (μkat/L)</b> |                  |                  |
| Week 7–17                                      | <0.15a           | 0.50 (0.41–0.58) |
| Week 17–24                                     | <0.15a           | 0.55 (0.49–0.61) |
| Week 24–28                                     | <0.15a           | 0.54 (0.44–0.63) |
| Week 28–31                                     | <0.15a           | 0.39 (0.37–0.40) |
| Week 31–34                                     | <0.15a           | 0.42 (0.38–0.46) |
| Week 34–38                                     | <0.15a           | 0.41 (0.38–0.44) |
| Predelivery                                    | <0.15a           | 0.36 (0.33–0.39) |
| Postpartum                                     | 0.19 (0.17–0.20) | 1.10 (1.00–1.19) |
| <b>Albumin (g/L)</b>                           |                  |                  |
| Week 7–17                                      | 32.2 (30.9–33.5) | 43.2 (42.6–43.8) |
| Week 17–24                                     | 27.9 (27.4–28.4) | 36.9 (36.4–37.3) |
| Week 24–28                                     | 27.0 (26.5–27.4) | 34.6 (33.8–35.4) |
| Week 28–31                                     | 25.1 (24.3–25.9) | 33.7 (33.3–34.0) |
| Week 31–34                                     | 24.4 (23.5–25.3) | 33.7 (33.1–34.3) |
| Week 34–38                                     | 23.1 (21.9–24.4) | 33.8 (32.5–35.2) |
| Predelivery                                    | 24.0 (23.0–24.9) | 38.2 (34.4–42.0) |
| Postpartum                                     | 37.0 (36.4–37.6) | 47.2 (46.6–47.8) |
| <b>Alkaline phosphatase (μkat/L)</b>           |                  |                  |
| Week 7–17                                      | 0.58 (0.53–0.63) | 1.33 (1.20–1.46) |
| Week 17–24                                     | 0.65 (0.63–0.68) | 1.75 (1.37–2.14) |
| Week 24–28                                     | 0.77 (0.74–0.81) | 1.92 (1.66–2.18) |
| Week 28–31                                     | 0.88 (0.78–0.98) | 1.98 (1.75–2.21) |
| Week 31–34                                     | 1.11 (1.02–1.20) | 2.96 (2.55–3.36) |
| Week 34–38                                     | 1.46 (1.23–1.68) | 3.81 (3.41–4.21) |
| Predelivery                                    | 1.64 (1.37–1.91) | 4.95 (4.70–5.19) |
| Postpartum                                     | 0.87 (0.69–1.04) | 2.74 (2.30–3.18) |
| <b>Amylase (pancreas) (μkat/L)</b>             |                  |                  |
| Week 7–17                                      | 0.22 (0.19–0.25) | 0.73 (0.65–0.81) |
| Week 17–24                                     | 0.26 (0.23–0.29) | 0.78 (0.69–0.86) |
| Week 24–28                                     | 0.25 (0.20–0.30) | 0.84 (0.67–1.00) |
| Week 28–31                                     | 0.25 (0.21–0.29) | 0.66 (0.62–0.70) |
| Week 31–34                                     | 0.24 (0.19–0.29) | 0.93 (0.80–1.05) |
| Week 34–38                                     | 0.25 (0.20–0.30) | 0.82 (0.76–0.87) |
| Predelivery                                    | 0.25 (0.20–0.27) | 0.70 (0.61–0.79) |
| Postpartum                                     | 0.25 (0.23–0.28) | 0.65 (0.60–0.70) |
| <b>Apolipoprotein A1 (g/L)</b>                 |                  |                  |
| Week 7–17                                      | 1.16 (1.00–1.31) | 2.47 (2.21–2.74) |
| Week 17–24                                     | 1.48 (1.40–1.56) | 2.53 (2.46–2.60) |
| Week 24–28                                     | 1.51 (1.41–1.61) | 2.47 (2.39–2.55) |
| Week 28–31                                     | 1.43 (1.16–1.70) | 2.56 (2.49–2.63) |
| Week 31–34                                     | 1.40 (1.14–1.65) | 2.69 (2.58–2.81) |
| Week 34–38                                     | 1.45 (1.34–1.55) | 2.62 (2.46–2.77) |
| Predelivery                                    | 1.32 (1.11–1.53) | 2.68 (2.50–2.86) |
| Postpartum                                     | 1.17 (1.11–1.23) | 2.00 (1.93–2.05) |
| <b>Apolipoprotein B (g/L)</b>                  |                  |                  |
| Week 7–17                                      | 0.53 (0.51–0.56) | 1.23 (1.17–1.30) |
| Week 17–24                                     | 0.66 (0.60–0.71) | 1.88 (1.65–2.10) |
| Week 24–28                                     | 0.67 (0.55–0.79) | 2.27 (1.96–2.57) |

(continued)



**Table 17.5** (continued)

|                            | Lower limit      | Upper limit      |
|----------------------------|------------------|------------------|
| Week 28–31                 | 0.73 (0.64–0.81) | 2.32 (2.06–2.58) |
| Week 31–34                 | 0.81 (0.62–1.00) | 2.62 (2.21–3.02) |
| Week 34–38                 | 0.85 (0.78–0.93) | 2.38 (2.22–2.53) |
| Predelivery                | 0.75 (0.63–0.87) | 2.50 (2.38–2.61) |
| Postpartum                 | 0.52 (0.40–0.63) | 1.37 (1.29–1.45) |
| <b>AST (μkat/L)</b>        |                  |                  |
| Week 7–17                  | 0.15 (0.13–0.18) | 0.66 (0.57–0.76) |
| Week 17–24                 | 0.17 (0.15–0.18) | 0.55 (0.48–0.62) |
| Week 24–28                 | 0.19 (0.17–0.20) | 0.56 (0.44–0.68) |
| Week 28–31                 | 0.19 (0.16–0.21) | 0.47 (0.43–0.50) |
| Week 31–34                 | 0.21 (0.19–0.23) | 0.49 (0.47–0.51) |
| Week 34–38                 | 0.21 (0.20–0.22) | 0.53 (0.46–0.59) |
| Predelivery                | 0.22 (0.21–0.24) | 0.56 (0.52–0.60) |
| Postpartum                 | 0.15 (0.12–0.18) | 0.70 (0.67–0.73) |
| <b>Bilirubin (μmol/L)</b>  |                  |                  |
| Week 7–17                  | 3.5 (<3.0–4.4)   | 22.4 (18.8–26.0) |
| Week 17–24                 | <3.0a            | 13.9 (12.2–15.6) |
| Week 24–28                 | <3.0a            | 17.8 (14.3–21.4) |
| Week 28–31                 | <3.0a            | 19.7 (15.4–24.1) |
| Week 31–34                 | <3.0a            | 17.1 (15.0–19.2) |
| Week 34–38                 | <3.0a            | 18.6 (15.7–21.4) |
| Predelivery                | <3.0a            | 19.4 (14.9–23.9) |
| Postpartum                 | 3.3 (<3.0–3.8)   | 30.9 (22.8–39.0) |
| <b>Calcium (mmol/L)</b>    |                  |                  |
| Week 7–17                  | 2.18 (2.12–2.23) | 2.53 (2.50–2.57) |
| Week 17–24                 | 2.08 (2.04–2.11) | 2.45 (2.41–2.50) |
| Week 24–28                 | 2.04 (1.99–2.08) | 2.40 (2.36–2.43) |
| Week 28–31                 | 2.07 (2.03–2.11) | 2.41 (2.33–2.49) |
| Week 31–34                 | 2.05 (1.99–2.10) | 2.38 (2.37–2.40) |
| Week 34–38                 | 2.04 (1.96–2.11) | 2.41 (2.39–2.43) |
| Predelivery                | 1.98 (1.91–2.05) | 2.46 (2.42–2.50) |
| Postpartum                 | 2.06 (1.90–2.22) | 2.57 (2.51–2.63) |
| <b>Chloride (mmol/L)</b>   |                  |                  |
| Week 7–17                  | 100 (100–101)    | 107 (107–107)    |
| Week 17–24                 | 97 (95–99)       | 107 (107–107)    |
| Week 24–28                 | 99 (97–100)      | 108 (107–108)    |
| Week 28–31                 | 99 (97–100)      | 108 (108–109)    |
| Week 31–34                 | 97 (95–100)      | 108 (107–108)    |
| Week 34–38                 | 97 (95–100)      | 109 (107–110)    |
| Predelivery                | 95 (91–99)       | 108 (107–108)    |
| Postpartum                 | 100 (100–101)    | 108 (107–109)    |
| <b>Creatinine (μmol/L)</b> |                  |                  |
| Week 7–17                  | 36 (34–39)       | 62 (61–63)       |
| Week 17–24                 | 34 (31–38)       | 58 (57–59)       |
| Week 24–28                 | 32 (27–36)       | 62 (60–63)       |
| Week 28–31                 | 32 (28–36)       | 56 (55–58)       |
| Week 31–34                 | 34 (32–36)       | 58 (57–60)       |
| Week 34–38                 | 33 (31–36)       | 60 (56–64)       |
| Predelivery                | 31 (25–36)       | 72 (67–78)       |
| Postpartum                 | 48 (43–53)       | 86 (79–93)       |
| <b>Cyc-C (mg/L)</b>        |                  |                  |
| Week 7–17                  | 0.41 (0.39–0.43) | 0.62 (0.61–0.64) |
| Week 17–24                 | 0.46 (0.45–0.46) | 0.71 (0.68–0.73) |

**Table 17.5** (continued)

|                           | Lower limit      | Upper limit         |
|---------------------------|------------------|---------------------|
| Week 24–28                | 0.47 (0.44–0.50) | 0.76 (0.74–0.78)    |
| Week 28–31                | 0.50 (0.48–0.51) | 0.82 (0.79–0.84)    |
| Week 31–34                | 0.50 (0.46–0.55) | 0.98 (0.94–1.02)    |
| Week 34–38                | 0.58 (0.53–0.63) | 1.30 (1.23–1.37)    |
| Predelivery               | 0.63 (0.53–0.73) | 1.70 (1.36–2.04)    |
| Postpartum                | 0.54 (0.49–0.59) | 1.00 (0.93–1.07)    |
| <b>Ferritin (µg/L)</b>    |                  |                     |
| Week 7–17                 | 7.1 (6.3–7.9)    | 106.4 (83.9–128.9)  |
| Week 17–24                | 4.1 (3.1–5.1)    | 65.6 (46.5–84.7)    |
| Week 24–28                | 3.8 (3.0–4.6)    | 49.8 (37.9–61.6)    |
| Week 28–31                | 4.2 (3.9–4.5)    | 39.0 (29.5–48.5)    |
| Week 31–34                | 4.3 (3.9–4.7)    | 40.5 (33.8–47.2)    |
| Week 34–38                | 4.8 (4.3–5.2)    | 43.5 (38.7–48.2)    |
| Predelivery               | 5.0 (4.1–6.0)    | 60.5 (57.5–63.4)    |
| Postpartum                | 6.9 (4.7–9.1)    | 139.0 (103.1–174.8) |
| <b>GGT (µkat/L)</b>       |                  |                     |
| Week 7–17                 | 0.12 (0.11–0.13) | 0.58 (0.52–0.64)    |
| Week 17–24                | 0.09 (0.08–0.10) | 0.36 (0.31–0.40)    |
| Week 24–28                | 0.09 (0.08–0.10) | 0.40 (0.34–0.47)    |
| Week 28–31                | 0.09 (0.07–0.10) | 0.41 (0.35–0.47)    |
| Week 31–34                | 0.08 (0.06–0.10) | 0.43 (0.40–0.46)    |
| Week 34–38                | 0.09 (0.07–0.11) | 0.40 (0.32–0.48)    |
| Predelivery               | 0.09 (0.07–0.10) | 0.65 (0.47–0.83)    |
| Postpartum                | 0.11 (0.10–0.12) | 0.58 (0.38–0.78)    |
| <b>Iron (µmol/L)</b>      |                  |                     |
| Week 7–17                 | 8.7 (6.9–10.5)   | 37.0 (34.5–39.5)    |
| Week 17–24                | 7.9 (4.8–10.9)   | 31.9 (29.1–34.7)    |
| Week 24–28                | 8.0 (4.7–11.3)   | 50.0 (37.6–62.3)    |
| Week 28–31                | 7.6 (6.6–8.7)    | 37.5 (31.8–43.2)    |
| Week 31–34                | 6.9 (5.6–8.2)    | 36.4 (30.4–42.3)    |
| Week 34–38                | 7.6 (7.3–7.9)    | 34.5 (31.7–37.3)    |
| Predelivery               | 8.0 (5.5–10.6)   | 32.9 (29.8–36.0)    |
| Postpartum                | 7.9 (6.8–9.1)    | 30.1 (25.3–34.9)    |
| <b>LDH (µkat/L)</b>       |                  |                     |
| Week 7–17                 | 1.60 (1.58–1.63) | 5.72 (3.57–7.86)    |
| Week 17–24                | 1.38 (1.24–1.51) | 2.52 (2.42–2.63)    |
| Week 24–28                | 1.28 (1.13–1.42) | 3.11 (2.59–3.64)    |
| Week 28–31                | 1.37 (1.13–1.49) | 2.87 (2.51–3.24)    |
| Week 31–34                | 1.42 (1.36–1.49) | 3.17 (2.74–3.60)    |
| Week 34–38                | 1.41 (1.34–1.48) | 2.55 (2.48–2.61)    |
| Predelivery               | 1.64 (1.60–1.67) | 2.80 (2.74–2.86)    |
| Postpartum                | 1.58 (1.48–1.68) | 3.43 (3.07–3.78)    |
| <b>Magnesium (mmol/L)</b> |                  |                     |
| Week 7–17                 | 0.70 (0.69–0.71) | 0.96 (0.88–1.059)   |
| Week 17–24                | 0.66 (0.65–0.66) | 0.87 (0.84–0.90)    |
| Week 24–28                | 0.63 (0.63–0.63) | 0.91 (0.86–0.97)    |
| Week 28–31                | 0.63 (0.63–0.64) | 0.91 (0.88–0.94)    |
| Week 31–34                | 0.64 (0.64–0.64) | 0.90 (0.84–0.97)    |
| Week 34–38                | 0.57 (0.50–0.65) | 0.87 (0.84–0.90)    |
| Predelivery               | 0.64 (0.63–0.65) | 0.94 (0.91–0.96)    |
| Postpartum                | 0.68 (0.66–0.71) | 0.99 (0.92–1.06)    |

(continued)

**Table 17.5** (continued)

|                               | Lower limit         | Upper limit         |
|-------------------------------|---------------------|---------------------|
| <b>Phosphate (mmol/L)</b>     |                     |                     |
| Week 7–17                     | 0.85 (0.80–0.90)    | 1.65 (1.43–1.86)    |
| Week 17–24                    | 0.84 (0.74–0.95)    | 1.45 (1.41–1.48)    |
| Week 24–28                    | 0.81 (0.67–0.95)    | 1.47 (1.43–1.51)    |
| Week 28–31                    | 0.77 (0.70–0.85)    | 1.44 (1.38–1.49)    |
| Week 31–34                    | 0.84 (0.72–0.95)    | 1.42 (1.35–1.49)    |
| Week 34–38                    | 0.85 (0.80–0.90)    | 1.45 (1.41–1.50)    |
| Predelivery                   | 0.89 (0.86–0.92)    | 1.50 (1.43–1.57)    |
| Postpartum                    | 1.00 (0.89–1.12)    | 1.80 (1.62–1.99)    |
| <b>Potassium (mmol/L)</b>     |                     |                     |
| Week 7–17                     | 3.24 (3.14–3.35)    | 4.86 (4.61–5.12)    |
| Week 17–24                    | 3.26 (3.06–3.45)    | 4.60 (4.49–4.72)    |
| Week 24–28                    | 3.27 (3.17–3.38)    | 4.62 (4.57–4.68)    |
| Week 28–31                    | 3.46 (3.40–3.52)    | 4.74 (4.54–4.93)    |
| Week 31–34                    | 3.30 (3.16–3.44)    | 5.16 (4.99–5.33)    |
| Week 34–38                    | 3.32 (3.19–3.46)    | 5.09 (4.75–5.43)    |
| Predelivery                   | 3.41 (3.35–3.47)    | 5.46 (5.23–5.68)    |
| Postpartum                    | 3.48 (3.41–3.55)    | 5.06 (4.88–5.23)    |
| <b>Sodium (mmol/L)</b>        |                     |                     |
| Week 7–17                     | 133.2 (131.7–134.7) | 140.5 (139.5–141.5) |
| Week 17–24                    | 128.5 (127.3–129.8) | 140.0 (139.5–140.5) |
| Week 24–28                    | 129.2 (127.7–130.7) | 139.3 (139.1–139.5) |
| Week 28–31                    | 129.9 (128.2–131.6) | 140.2 (138.7–141.7) |
| Week 31–34                    | 127.0 (122.9–131.1) | 139.1 (139.0–139.3) |
| Week 34–38                    | 127.0 (123.2–130.7) | 140.2 (139.3–141.2) |
| Predelivery                   | 124.0 (120.6–127.4) | 140.4 (139.3–141.4) |
| Postpartum                    | 134.0 (132.4–135.7) | 143.8 (143.5–144.1) |
| <b>Transferrin (g/L)</b>      |                     |                     |
| Week 7–17                     | 1.92 (1.76–2.08)    | 3.85 (3.44–4.26)    |
| Week 17–24                    | 2.20 (2.04–2.36)    | 4.34 (4.14–4.54)    |
| Week 24–28                    | 2.72 (2.68–2.77)    | 4.36 (4.23–4.50)    |
| Week 28–31                    | 2.86 (2.82–2.91)    | 4.78 (4.69–4.88)    |
| Week 31–34                    | 2.94 (2.86–3.02)    | 5.09 (5.05–5.13)    |
| Week 34–38                    | 2.88 (2.76–3.00)    | 5.12 (4.72–5.52)    |
| Predelivery                   | 2.59 (2.47–2.71)    | 5.53 (5.23–5.83)    |
| Postpartum                    | 1.73 (1.54–1.91)    | 3.39 (3.07–3.71)    |
| <b>Triglycerides (mmol/L)</b> |                     |                     |
| Week 7–17                     | 0.55 (0.46–0.63)    | 3.08 (2.21–3.95)    |
| Week 17–24                    | 0.89 (0.73–1.05)    | 4.32 (3.76–4.89)    |
| Week 24–28                    | 1.09 (0.92–1.25)    | 3.63 (3.32–3.94)    |
| Week 28–31                    | 1.12 (0.96–1.29)    | 4.98 (4.27–5.69)    |
| Week 31–34                    | 1.52 (1.41–1.62)    | 4.79 (4.15–5.43)    |
| Week 34–38                    | 1.62 (1.28–1.97)    | 5.12 (4.72–5.52)    |
| Predelivery                   | 1.51 (1.29–1.72)    | 5.87 (5.22–6.52)    |
| Postpartum                    | 0.51 (0.48–0.54)    | 3.53 (2.75–4.32)    |
| <b>TSH (mU/L)</b>             |                     |                     |
| Week 7–17                     | 0.09 (0.00–0.26)    | 3.39 (3.02–3.76)    |
| Week 17–24                    | 0.37 (0.24–0.49)    | 3.40 (2.62–4.19)    |
| Week 24–28                    | 0.39 (0.27–0.51)    | 3.88 (3.27–4.50)    |
| Week 28–31                    | 0.23 (0.00–0.48)    | 2.83 (2.65–3.02)    |
| Week 31–34                    | 0.40 (0.26–0.53)    | 3.88 (3.18–4.59)    |
| Week 34–38                    | 0.38 (0.24–0.51)    | 4.04 (2.95–5.13)    |
| Predelivery                   | 0.78 (0.52–1.04)    | 5.33 (4.28–6.39)    |

**Table 17.5** (continued)

|                                             | Lower limit         | Upper limit         |
|---------------------------------------------|---------------------|---------------------|
| Postpartum                                  | 0.22 (0.00–0.49)    | 3.19 (2.67–3.70)    |
| <b>Urate (<math>\mu\text{mol/L}</math>)</b> |                     |                     |
| Week 7–17                                   | 121.3 (105.3–137.3) | 314.2 (278.9–349.5) |
| Week 17–24                                  | 147.8 (130.2–165.4) | 293.9 (274.3–313.6) |
| Week 24–28                                  | 143.2 (122.2–164.3) | 318.8 (299.0–338.5) |
| Week 28–31                                  | 137.5 (113.8–161.3) | 289.2 (283.6–294.9) |
| Week 31–34                                  | 153.5 (139.9–167.0) | 353.7 (327.2–380.3) |
| Week 34–38                                  | 185.9 (176.8–195.0) | 373.4 (345.5–401.3) |
| Predelivery                                 | 202.3 (185.4–219.3) | 401.2 (385.6–416.7) |
| Postpartum                                  | 175.3 (142.2–208.3) | 437.9 (417.3–458.6) |
| <b>Urea (<math>\text{mmol/L}</math>)</b>    |                     |                     |
| Week 7–17                                   | 2.07 (1.93–2.21)    | 4.21 (3.97–4.45)    |
| Week 17–24                                  | 1.66 (1.36–1.96)    | 4.50 (4.07–4.94)    |
| Week 24–28                                  | 1.60 (1.32–1.87)    | 4.18 (4.05–4.32)    |
| Week 28–31                                  | 1.51 (1.12–1.90)    | 3.63 (3.29–3.96)    |
| Week 31–34                                  | 1.72 (1.62–1.83)    | 3.65 (3.55–3.75)    |
| Week 34–38                                  | 1.70 (1.66–1.74)    | 3.97 (3.88–4.05)    |
| Predelivery                                 | 1.62 (1.43–1.81)    | 4.88 (4.66–5.11)    |
| Postpartum                                  | 2.80 (2.24–3.37)    | 7.17 (6.80–7.53)    |

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a The 90% confidence interval could not be calculated as the instrument did not report ALT values  $<0.15 \mu\text{kat/L}$  and bilirubin values  $<3.0$  and several test results were  $<0.15$  and  $<3.0$ , respectively

## 17.5.1 Laboratory Findings

### 17.5.1.1 Liver and Pancreatic Enzymes

Marcus, in 1930, is credited with the first clinical diagnosis of AP in pregnancy with the aid of diastase and amylase studies [206]. Pregnancy-related hematological and biochemical alterations interfere with the interpretation of diagnostic tests and assessment of the severity of AP (Table 17.5). In healthy pregnant subjects, low amylase levels are most frequent between the 8th and 16th weeks but rise steadily in the later months, reaching the normal range at full term [212, 213].

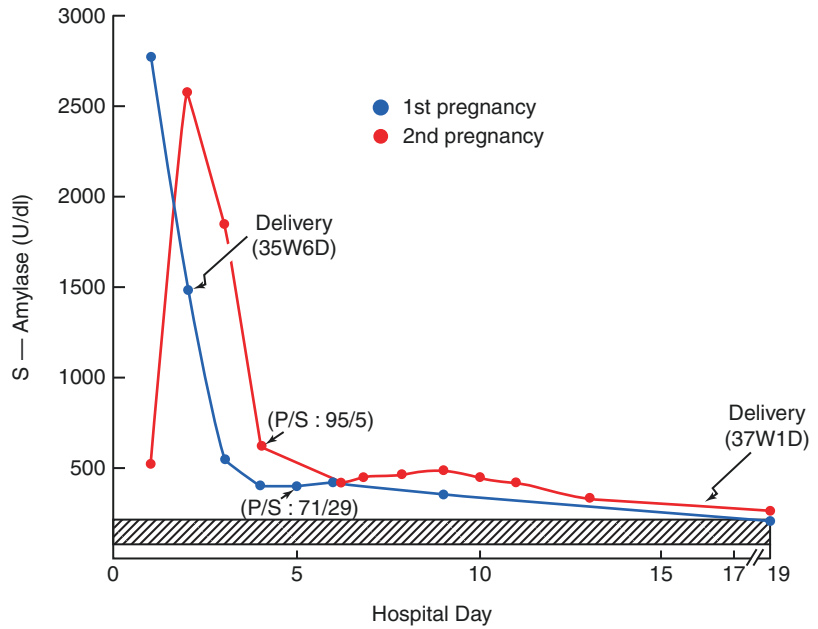
Laboratory investigations are the same as in nonpregnant and rely on at least a three-fold elevation of serum amylase and lipase levels.

The total serum amylase level rises within 6–12 h of the onset of the disease and usually remains elevated for 3–5 days. Serum lipase ele-

vates on the first day and remains elevated for up to 2 weeks. In terms of diagnostic accuracy, specificity, and sensitivity in the general population, lipase is superior to amylase [214, 215] despite not being specific to the pancreas. Enzyme concentrations are similar in nonpregnant and pregnant women, and an increase in either is suggestive of AP in pregnancy [216]. Elevating serum alanine aminotransferase levels to  $>3$  times the upper limit is very sensitive for biliary AP in the nonpregnant population [217] and could be used in pregnancy. The dynamics of amylase rise and fall depend on the severity and extension of pancreatic damage, and the relation between the AP cause and amylase curve is unknown (Fig. 17.10).

AP cannot be ruled out if a normal serum amylase level is detected. One reason is that the serum amylase may not increase with extensive pancreatic necrosis. Also, precise amylase values and several other laboratory parameters are unreliable, with a significant increase in plasma TG levels (see Sect. 17.5.1.2). In nonpregnant patients, normal amylase levels usually exclude the diagnosis of AP, except for hyperlipidemic AP, acute exac-

**Fig. 17.10** Changes in the serum amylase level during hospital admission. The shaded horizontal area indicates the normal range for serum amylase. P/S, the ratio of the pancreas to salivary amylase isozymes. (Reproduced with permission from [218])



erbaration of chronic pancreatitis, and examinations in the delayed course of AP [219]. Therefore, the urine amylase level may be more helpful. Morphine administration can change serum amylase and urinary diastase values. Morphine causes spasms of the sphincter of Oddi with obstruction of pancreatic drainage. In terms of diagnostic accuracy, lipase has proven superior to amylase in AP [214].

No enzyme assay has a predictive role in determining the severity or etiology of AP in pregnancy [220].

Once the diagnosis of AP is established, daily measurements of enzymes have no value in assessing the clinical progress or ultimate prognosis. A persistently raised serum amylase activity may suggest the presence of a pancreatic pseudocyst. Due to the extreme rarity, there are no data available about amylase and lipase dynamics for the early postpartum period.

Liver tests in pregnant women with biliary AP are frequently normal. The transaminase levels are less than 5× the normal upper limits in 89%

and less than 3× the normal upper limits in 80%. The increased metabolism of maternal transaminases by the placenta could lead to relatively normal maternal levels of liver enzymes [29].

Laboratory abnormalities consistent with AFLP include mild elevation of ALT and AST to 200–300 IU/L [221], prolonged prothrombin time and partial thromboplastin time, decreased fibrinogen, acute renal failure, severe hypoglycemia, a bilirubin level of 1–10 mg/dL, and leukocytosis. In pregnant women with AP and AFLP, elevated serum lipase levels are present in 91% [203]. The diagnosis of LCHAD deficiency in newborns can save lives; therefore, all women with AFLP and their children should have molecular tests for LCHAD [222, 223].

Gamma-glutamyl transpeptidase (GGT) levels either are unchanged or fall slightly during gestation. An elevated GGT level can help us evaluate the history of alcohol use during pregnancy, as patients might not be coming forth due to associated stigmata [224].

### 17.5.1.2 Serum Lipids

HTG-induced AP is triggered when TG levels exceed 1000 mg/dL (10 mmol/L) unless accompanied by lactescent (milky) serum [41, 176], found in 45% of patients [41]. In severe HTG (serum TG level >2000 mg/dL), there is a



significant risk of AP [225]. A normal lipidogram across pregnancy is presented in Fig. 3.4. Chylomicrons are formed at these high TG levels, and serum becomes lactescent. TG values of even 3810 mg/dL were encountered [226]. In contrast, mild-to-moderate elevations in TGs (2–10 mmol/L) are extremely common in the early phase of AP of any etiology. One study noted such elevations in 47% of randomly selected patients presenting with AP [50]. Mild-to-moderate elevations of TGs were felt more likely to be an epiphenomenon of the AP rather than a cause [50]. Chylomicrons are the product of dietary fat absorption. Enforced abstinence from eating after a diagnosis of AP may allow rapid metabolism of the TG-rich chylomicrons. Severe elevations (>20 mmol/L) were found in 10% of patients, but levels rapidly fell in most patients within 72 h of presentation. Therefore, a delay in the presentation or consideration of diagnosis can lead to false conclusions about etiology. TG levels remained mildly elevated for up to 15 days, probably reflecting an underlying lipid disorder [50]. Some recommend that a lipemic blood sample found at any stage during pregnancy should be considered as potentially indicative of partial LPL deficiency [227]. Lipid analysis requires direct measurement through centrifugation or immunoprecipitation.

### 17.5.1.3 Serum Calcium and Parathormone

Serum calcium levels should be obtained in pregnant women with persistent nausea, vomiting, and abdominal pain, especially when AP is suspected [228].

PHPT is diagnosed with elevated calcium and elevated or normal intact PTH level [229]. Maternal serum calcium falls by about 10% in pregnancy. Therefore, it may be prudent to draw ionized calcium when evaluating calcium. During pregnancy, there is an increase in extracellular volume and a 20% decrease in albumin, resulting in factitiously low calcium (lower

10%), whereas the ionized calcium remains unchanged [191]. Intact serum PTH represents the N-terminal fragment of PTH. This is the recommended level, given that the C-terminal or standard PTH level may be falsely elevated in patients with renal impairment due to the extended half-life and may be mildly elevated in the elderly [69]. An elevated serum PTH level does not necessarily indicate PHPT (especially in pregnant women), and a normal level does not exclude it. Therefore, the serum PTH level must be evaluated as a function of the serum calcium level. Patients with hypercalcemia, normal renal function, and an elevated serum PTH level almost certainly have primary HPT. However, even when the serum PTH level is normal in these patients, PHPT should still be suspected since hypercalcemia should suppress parathyroid gland function and reduce the serum PTH level to below normal. Therefore, detectable amounts of PTH in the blood of patients with hypercalcemia are compatible with PHPT. In patients with normal PTH levels, the PTH molecule has undergone cleavage by the liver and kidney, reducing its levels in the peripheral veins. Fasting serum phosphate (hypophosphatemia, <2.5 mg/dL) and the urinary cyclic adenosine monophosphate levels help in recognizing PHPT. Total serum calcium concentration >10.1 mg/dL (2.52 mmol/L) during the second or 8.8 mg/dL (2.2 mmol/L) during the third trimester is diagnostic for PHPT. Hypercalcemia with values higher than 13 mg/mL in the presence of a palpable neck mass should raise a strong suspicion of parathyroid carcinoma.

Hypercalcemia should be suspected when samples to obtain a coagulation profile result in clotting and cannot be analyzed. Calcium is required for coagulation factors to bind to phospholipids, and this binding is typically arrested in laboratory studies with sodium citrate. For a typical laboratory specimen, whole blood is collected using a test tube with a fixed amount of sodium citrate in the ratio of one part citrate solution to nine parts of whole blood. Before analysis, a fixed amount of calcium is added back to the sample to bind to the citrate in the tube, allowing clotting studies to be evaluated. The amount of

citrate in collection tubes accounts for normal ranges of calcium. In severe hypercalcemia, there is no standardized method for adding citrate solution to overcome it, and the results are not standardized or validated. Therefore, evaluations of coagulation studies are deferred until the patient's serum calcium is lowered. Coagulopathy is excluded based on stable platelet studies, a peripheral smear without schistocytes, thromboelastography, and no clinical evidence of bleeding.

Only 50% of PHPT-induced AP in pregnancy has hypercalcemia [230]. Hypocalcemia is a sign of SAP and delays the diagnosis of PHPT-induced AP [230]. Serial monitoring of serum calcium levels and PTH should be performed if PHPT is suspected. Approximately 20–30% of PHPT patients in the general population have multiple endocrine neoplasia (MEN) type IIa [231].

The patient diagnosed with PHPT during pregnancy should be investigated for MEN-IIa syndrome.

#### 17.5.1.4 Other Serum Markers

Serum CRP at 48 h is the best available laboratory marker of AP severity.

Urinary trypsinogen activation peptides within 12–24 h of onset of AP can predict the severity of AP.

MPV, WBC, and CRP can differentiate between HTG and HTG-induced AP in pregnancy [232]. Also, MPV is a good indicator of the severity of HTG-induced AP [232]. There is a stimulation of megakaryopoiesis in the early stages of the inflammatory process, producing many young and large platelets with high procoagulation potential. In addition, MPV increases during pregnancy due to hormonal and metabolic changes [233]. Thrombocytopenia is both common during pregnancy and frequent at the onset of AP. Thrombocytopenia can lead to enhanced thrombopoiesis, which increases the quantity of highly reactive large-sized platelets.

Increased LDH has a high AUC (0.777), with a cutoff value of 263 IU/L and a specificity of 0.879, which can be treated as one of the best predictors for SAP in AP during pregnancy [234].

The lymphocyte-to-monocyte ratio (LMR) counts are significantly decreased in the SAP group in pregnancy. Lower LMR was an independent SAP factor in pregnancy, with a cutoff value of 1.51 [234].

Patients examined within 48–72 h after the onset of AP have fasting hyperglycemia, hyperglucagonemia, and relative hypoinsulinemia. These changes gradually reverse with recovery from the acute episode, reaching normal within 15 days [235]. Therefore, it is not always clear whether the pregnant patient has gestational DM or hyperglycemia due to AP. Serum glucose levels should be checked several weeks and months after the episode of AP and OGTT made if not performed during pregnancy before the attack of AP.

#### 17.5.1.5 Confounding Laboratory Findings

##### Amylase/Lipase

In the general population, 16–25% of patients with diabetic ketoacidosis may have elevated pancreatic enzymes and TGs, circumstances less reliable diagnosis of AP based only on biochemical parameters [236]. The rise of amylase and lipase levels exceeded the expected increased values due to the slight reduction in the renal function in the preeclamptic. However, it indicates a possible concomitant pancreatic injury [237].

##### Triglycerides

Elevated TG levels can alter sodium, amylase, and LDL serum levels. Pseudohyponatremia results in excess TG, which displaces water-containing sodium [238]. Ultracentrifugation separates the aqueous phase and measures the accurate sodium levels [238]. HTG levels >500 mg/dL may cause a falsely normal amylase due to interference with a calorimetric reading of the assay or the presence of an interfering inhibitor. Although the exact inhibitor is unknown, it does not seem to be TG itself, as removing excess

serum lipids by ultracentrifugation does not eliminate the inhibition of amylase activity [239]. Lipemia may affect an automated analysis of other parameters, such as glucose, liver enzymes, urea, creatinine, and total bilirubin, by altering light scattering, increasing the non-aqueous phase, and partitioning the polar non-polar phases [240]. This problem can be partially overcome by assaying serial sample dilutions [45, 239] or measuring *serum lipase or amylase-to-creatinine ratio* (ratio greater than 5% suggests AP) [241], neither of which is affected by HTG [45].

*Friedewald equation* [LDL-C in mg/dL = TC-HDL-C-(TG/5), LDL-C in mmol/L = TC-HDL-C-(TG/2.2)], used to determine LDL from TG levels, loses accuracy with high TG levels [242]; a commonly accepted upper limit is 400 mg/dL [243].

An intercurrent illness with acute phase inflammation with inflammatory response modifies the lipid and lipoprotein profile. Acute inflammation increases VLDL (TG) and reduces HDL-C and LDL-C. It is important to note that the lipoprotein response to intercurrent illness shares some features with DM type 2. The magnitude of modifica-

tions is usually proportional to the severity of the underlying illness [244], but proportionately smaller responses should also be anticipated in association with minor intercurrent illnesses. Therefore, HTG causes AP, while AP can further increase TG serum levels, creating a vicious cycle.

### Parathyroid Hormone

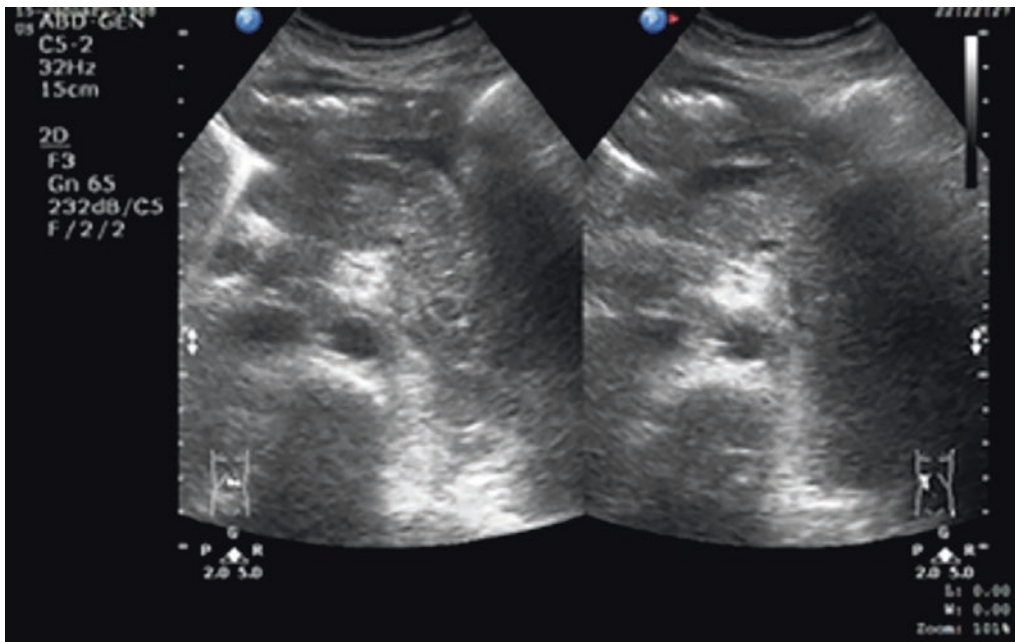
Parathyroid hormone levels may be falsely lowered due to hypoalbuminemia or suppressed by magnesium tocolysis [84].

#### 17.5.1.6 Ranson Criteria

There are several scoring systems in the general population, not for the diagnosis but the prognosis of AP. The most common in the general population, the Ranson scoring system, is rarely calculated and not validated in pregnancy [245, 246].

### 17.5.2 Transabdominal Ultrasound

Transabdominal ultrasound (US) is the initial imaging of choice in diagnosing AP (Fig. 17.11). It identifies or excludes biliary etiology, which



**Fig. 17.11** A bulky and inhomogeneous pancreas with the presence of peripancreatic fluid in keeping with acute pancreatitis at 8 weeks of pregnancy. (Reproduced with permission from [247] under the CC BY 3.0)



**Fig. 17.12** Sagittal section on the transabdominal US shows smaller (PC) and larger pseudocysts. Splenic vein (Sp.V) in cross section [56]

dictates further diagnostic workup and therapy depend. However, the sensitivity of the US in the general population in the detection of CBD stones is 20–38% [248, 249]. The US is limited by operator skill, patient obesity, and bowel dilation, primarily in peritonitis. However, it is helpful for focal accumulations larger than 2–3 cm and pancreatic pseudocysts—54% of the pseudocysts were diagnosed with US (Fig. 17.12).

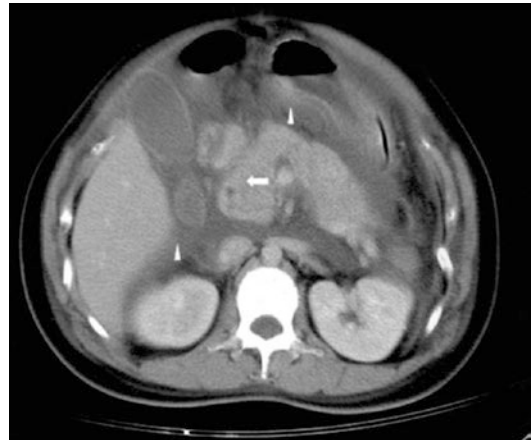
The additional US role is to estimate fetal growth and development (length of the femur) and fetal vitality by measuring indirect parameters, such as oligohydramnios.

### 17.5.3 Abdominal CT

Abdominal CT is used not only for the diagnosis but also to provide information about the severity of AP (Figs. 17.13, 17.14, 17.15, and 17.16). The accuracy of US and CT in diagnosing AFLP-induced AP in pregnancy was 58% [203].



**Fig. 17.13** Abdominal CT shows swelling of the pancreas with the adjacent fluid collection, suggestive of acute pancreatitis (arrow). (Reproduced with permission from [250] under the CC BY 3.0)



**Fig. 17.14** Abdominal CT in the 34th week of pregnancy with swelling of the pancreas and blurring of the mesenteric fat plane (arrow). Reactive paralytic ileus, fluid accumulation at bilateral anterior pararenal space, lesser sac, and extraperitoneal space are noted (arrowheads). (Reproduced with permission from [245])

### 17.5.4 Endoscopic Ultrasound

See Sect 16.2.5.5.

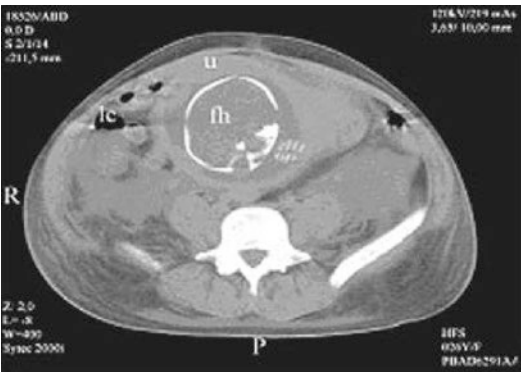
### 17.5.5 Abdominal MRI and MRCP

Magnetic resonance imaging (MRI) in pregnancy is indicated if the transabdominal US is not diagnostic (Fig. 17.17). 3D MRCP allows the reconstruction of overlapping slices of <1 mm [252,

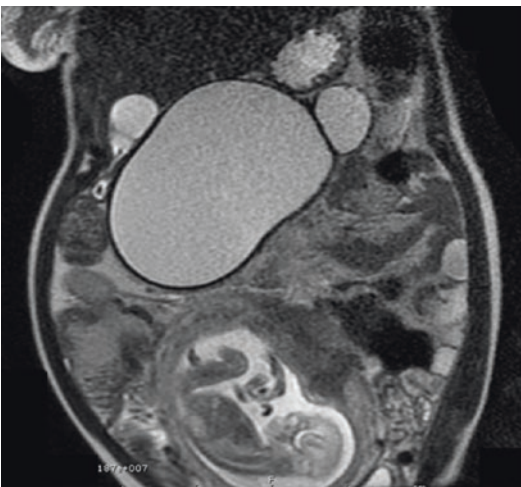




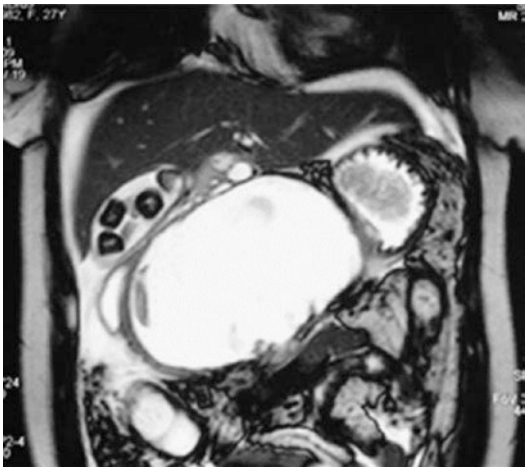
**Fig. 17.15** Pregnant uterus with surrounding fluid collection. *f* fetus, *dc* Douglas collection. (Reproduced with permission from [203])



**Fig. 17.16** Pregnant uterus. *u* uterus, *fh* fetal head, *lc* liquid collection. (Reproduced with permission from [203])



**Fig. 17.17** Abdominal MRI shows a 20 × 12 × 13 cm thick-walled lobular cyst arising from the proximal pancreatic body with a vital 19-week intrauterine pregnancy. (Reproduced with permission from [251])



**Fig. 17.18** MRCP shows a 14 × 7 cm pancreatic pseudocyst adjacent to the body of the pancreas, adherent to the posterior wall of the stomach with necrotic debris and gallstones. Gallbladder calculi are present. (Reproduced with permission from [257])

[253]. With an accuracy near 100% in determining the presence and the level of biliary obstruction in the general population, MRCP has replaced diagnostic ERCP [254, 255].

MRCP has high sensitivity and specificity for gallstones, CBD stones, and other biliary pathology. It can demonstrate the cause of biliary dilation, identifying a subset of patients who require immediate treatment. An accurate evaluation of the entire biliary system allows the detection of rare and complex pathologies, such as intrahepatic biliary stones, Mirizzi syndrome, and choledochal cysts (see Sect. 16.3). MRCP also obviates the need for intraoperative cholangiography. The third advantage is the evaluation of the pancreas and other locations with fluid collections [256] and pancreatic pseudocysts (Fig. 17.18).

### 17.5.6 Endoscopic Retrograde Cholangiopancreatography

See Sect 16.2.5.4.

### 17.5.7 Pancreatic Cyst Fluid Analysis

Cyst fluid analysis can differentiate cystic pancreatic neoplasms. In the general population,



amylase concentration <250 U/L rule out pseudocyst [258]. In addition, cyst fluid CA 19–9 level >50,000 U/mL has a sensitivity of 75% and a specificity of 90% for distinguishing mucinous tumors from other cystic lesions [259]. Furthermore, cyst fluid CEA >800 ng/mL has a sensitivity of 42.9% and a specificity of 95.2% for pancreatic MCNs [260]. When performing cyst aspiration, however, care must be taken to avoid spillage of cyst contents, resulting in pseudomyxoma peritonei [96], and uterine perforation, resulting in bleeding or fetal injury.

### 17.5.8 Parathyroid Gland Imaging

In patients with the laboratory findings of PHPT, imaging should follow to determine the etiology and location of the causative factor. In the general population, mediastinal ectopic parathyroid glands in PHPT have been as high as 20% [261]. The gold standard for imaging in the general population is a technetium-99m sestamibi scan. Technetium-99m sestamibi SPECT scanning with the gamma probe improves intraoperative localization [262]. However, this is contraindicated in pregnancy. The US is the preferred imaging modality, with 69% sensitivity and 94% specificity in diagnosing parathyroid adenoma [229]. Parathyroid glands >1.5 cm can be seen on CT. The sensitivity of MRI is higher than CT for detecting mediastinal lesions but lower than the technetium-99m sestamibi scan [263].

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## 17.6 Differential Diagnosis

### 17.6.1 Acute Pancreatitis

Differential diagnosis includes the same diseases from the nonpregnant population and some specific diseases during pregnancy. This is because the structures containing epithelium of Müllerian and mesonephric duct origin could produce amylase [264]. Intra-abdominally, these include the pancreas, fallopian tubes and ovarian cyst fluids, and some malignancies [265]. Therefore, hyperamylasemia can occur with perforated peptic

ulcer, perforated appendicitis, intestinal obstruction, mesenteric infarction, pulmonary embolism, pneumonia, myocardial infarction, lymphoma, hyperemesis gravidarum [266–268], and several tubo-ovarian pathologies, including ruptured ectopic pregnancy, salpingitis, pelvic inflammatory disease, ovarian papillary serous cystadenocarcinoma, ovarian adenosquamous carcinoma, ovarian endometrioid carcinoma, mucinous tumors, and surface papillary carcinoma [252, 253]. Hyperamylasemia associated with tubo-ovarian disease in which isoenzyme analysis was performed predominantly includes s-type amylase or an acidic variant [269], although p-type hyperamylasemia can be present. In addition, hemolysis of extravasated blood might cause an elevated pancreatic enzyme activity [270]. If hemorrhagic AP is wrongly suspected and the conservative approach is started, the prolonged bleeding from ruptured ectopic pregnancy can lead to hemorrhagic shock [271].

Lipase is also not specific to the pancreas. It is isolated in the tongue, esophagus, stomach, duodenum, small bowel, liver, lung, and adipose tissue [268]. Consequently, hyperlipasemia appears in cholecystitis, esophagitis, peptic ulcer disease, enteritis, peritonitis, and bowel obstruction/infarction [215, 268].

### 17.6.2 Hypercalcemia

The most common cause of hypercalcemic AP in pregnancy is PHPT, with many others (Table 17.3). However, with lytic bone lesions in the presence of hypercalcemia, the differential diagnosis is narrowed to bone fat necrosis secondary to AP, metastatic cancer (primary source uncertain), multiple myeloma [272], Paget disease (osteodystrophias deformans), primary lymphoma of the bone, leukemia, and rhabdomyosarcoma.

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## 17.7 Treatment

With the diagnosis of AP in pregnancy, assessment of severity based on clinical signs, blood tests, urinalysis, and imaging tests determine the

appropriate treatment. The treatment of AP is not standardized and is mainly supportive, and SAP is still a significant issue. The treatment goals are to avoid organ failure and infectious complications influencing fetal development. Pregnant women comprise 8% of hospitalizations for biliary AP among women in the USA [273].

## 17.7.1 Conservative Treatment

### 17.7.1.1 Supportive Measures

Treatment should include the following: (1) the treatment of the AP itself and (2) specific treatment/elimination of the cause of AP. The initial management of AP during pregnancy is similar to management in nonpregnant patients. It consists of fluid restoration, oxygen, analgesics, antiemetics, and monitoring of vital signs. Prompt and adequate IV fluid administration corrects the volume deficit and maintains basal fluid requirement [274–276]. The adequacy of fluid resuscitation is checked by monitoring the patient's vital signs. Necessary additional measures during pregnancy include fetal monitoring, attention to the choice of medications, and positioning of the mother to avoid inferior vena cava obstruction. Mild AP (MAP) treated conservatively usually resolves within 7 days. The severe course occurs in 10% of patients and should be managed in an intensive care unit (ICU) (see Sect. 17.7.1.4).

Parenteral nutrition is safe and necessary in pregnancy [25]. EN in SAP is better than TPN in patients without nausea and vomiting because EN helps to maintain the immune function of the gastrointestinal mucosa, protect the mucosal barrier, and improve the blood supply to the small intestine [274]. EN is delivered by nasojejunal tube and, if needed, should be supplemented by parenteral nutrition [277].

Many pharmacological agents (somatostatin, octreotide, *N*-acetylcysteine, gabexate mesylate, lexipafant, and probiotics) investigated in AP did not show a positive effect and should be avoided in pregnancy. Somatostatin inhibits both exocrine and endocrine portions, with pronounced effects in the early stage of AP. Somatostatin adminis-

tered in ten cases confirmed good outcomes without malformations and abnormal newborns [102]. With the permission of the patient and the agreement and signing of her family member, somatostatin is used in the early stage of SAP. Somatostatin should be applied continuously with IV infusion pumps with a low dose (150–250 µg/h) for 24–72 h and then reduced or withdrawn timely when hemodynamic stabilization occurs. Despite the encouraging results, somatostatin is not recommended for routine use because of its potential effect on the fetus. Cessation of oral feeding suppresses the exocrine function of the pancreas and prevents further pancreatic autodigestion. Bowel rest is associated with increased infectious complications, and TPN and EN have an essential role in the management of AP. Parenteral nutrition in pregnancy is considered safe and necessary when adequate oral nutrition is not possible. However, the frequency of complications from centrally inserted catheters is higher than in nonpregnant patients [278]. MAP does not require nutritional support due to the uncomplicated course, and a low-fat diet can start within 3–5 days.

### 17.7.1.2 Antibiotics

Prophylactic use of antibiotics is controversial, and the choice of antibiotics in pregnancy is challenging. Antibiotics have no role in treating MAP, normal CBD size, and no evidence for cholangitis. In contrast, broad-spectrum antibiotics could be beneficial in treating CT-proven necrotizing SAP [274–276]. The antibiotic prophylaxis might have a protective effect against non-pancreatic infections but failed to reduce mortality, infected necrosis, and the need for surgical intervention [279]. Due to the lack of evidence on the beneficial effect of antibiotics, a more conservative approach is recommended in pregnancy. Regardless of the initial drug regimen, therapy should be modified to reflect the organisms recovered in blood cultures and the patient's clinical status.

In the general population, only *imipenem* significantly reduced the risk of pancreatic infection [279]. The use of imipenem/cilastatin is indicated in necrotizing AP. However, dose adjustment in

pregnancy (FDA category C) should be considered even though the optimal dose is not recommended [280]. The pharmacokinetics of imipenem will change during pregnancy with a larger volume of distribution and faster total clearance from plasma [281]. *Metronidazole* passes freely across the placenta, but there is no increased teratogenic risk [282]. *Quinolones* (FDA category C) are alternatives to first-line antibiotic therapy.

### 17.7.1.3 Continuous Renal Replacement Therapy

Continuous renal replacement therapy (CRRT), including a variety of blood purification techniques that can slowly and steadily remove water, nitrogenous wastes, and even inflammatory mediators, has been widely used in patients with critical conditions such as SAP. CRRT is associated with significant improvement in pulmonary gas exchange, hemodynamic instability, azotemia control, fluid overload, and nutritional support in multiple organ failure (MOF) and acute renal failure [283]. Different modalities of continuous venovenous hemofiltration (CVVH) can prevent sepsis and improve survival in AP [284]. However, CVVH does not allow large molecules to pass through the hemofilter. Ronco et al. proposed a *peak concentration hypothesis* of MOF and found that CVVH combined with plasma filtration absorption techniques removes the excess circulating inflammatory mediators [285]. Hemoperfusion (HP) is another blood purification modality that can absorb pathogenic molecules in the blood by sorbent materials installed in the hemoperfusion cartridge. Unlike CVVH, HP is more effective for removing middle and large molecules and toxins bound to proteins. This treatment can effectively reduce the serum levels of proinflammatory cytokines during SAP and improvement of  $\text{PaO}_2/\text{FiO}_2$ . In the only pregnant patient with AP, the authors combined CVVH and broad-spectrum HP, assuming HP can effectively remove excess endogenous and exogenous pathogenic molecules. After the first 3 days of treatment, the general condition significantly improved, and laboratory parameters normalized [286]. After receiving HP and CVVH treatments,

the TG, CHOL, amylase, and lipase levels decreased dramatically (Fig. 17.19), explaining rapid recovery [286]. Moreover, the patient developed no side effects such as coagulopathy, hypotension, thrombocytopenia, or hypocalcemia.

### 17.7.1.4 Intensive Care Unit

In the general population, indicators for admission to ICU are [287] as follows:

- Need for fluid resuscitation,
- BMI >30 kg/m<sup>2</sup>,
- Pleural effusions,
- CRP >150 mg/L at 48 h,
- Necrosis of over 30% of the pancreas,
- Ranson criteria  $\geq 3$ .

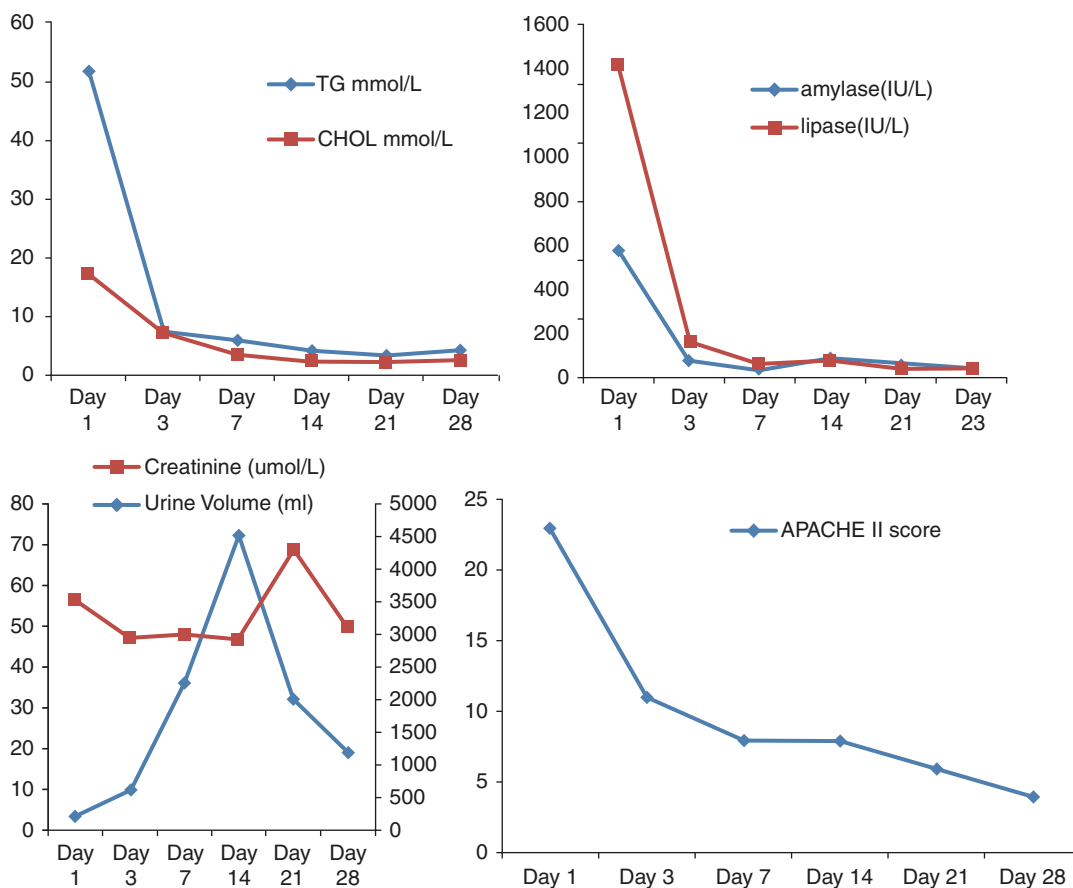
The third-space fluid sequestration is the most severe hemodynamic disorder leading to hypovolemia and organ hypoperfusion resulting in MOF. In volume-depleted patients, the essential treatment modality is an initial electrolyte infusion of 500–1000 mL/h [288]. Monitoring, hydration, and cardiovascular, renal, and respiratory functions are essential for detecting early volume overload and electrolyte disturbances. Organ failure may occur in 50% of patients. Early admission and management of critically ill obstetric patients in the ICU decrease maternal mortality and morbidity [289].

### 17.7.1.5 Hyperlipidemic Pancreatitis

The management goals of pregnant patients with HTG-induced AP should include decreasing the serum TG concentration and pancreatic activity while supplying maternal and fetal nutritional needs. Preconceptional control of TG levels may prevent or shorten the course of AP.

### Lipid-Lowering Diet

There is no consensus on the threshold of triglycerides for intervention in pregnancy, although 5.6 mmol/L has been suggested. When



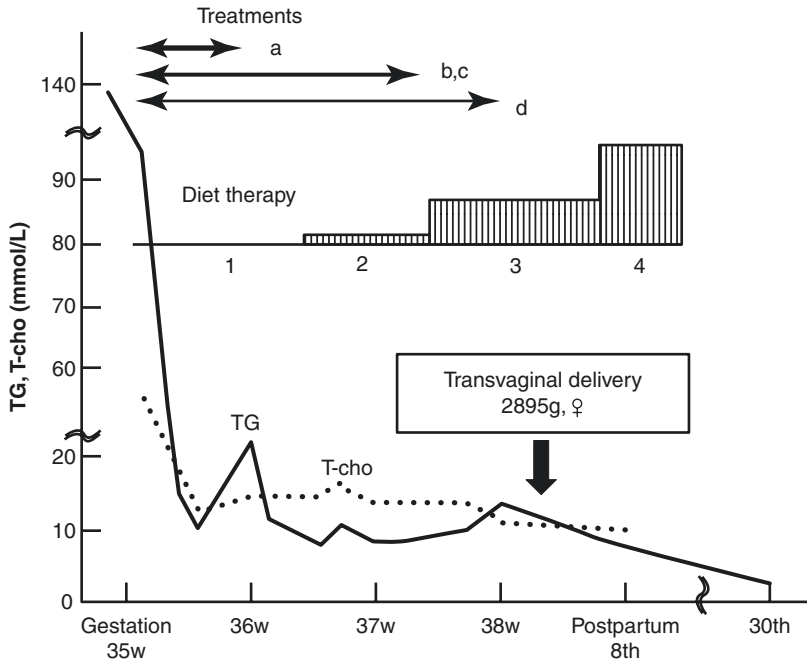
**Fig. 17.19** Changing tendency of triglyceride (TG), cholesterol (CHOL), amylase, lipase, renal function, and APACHE II score during the treatment. CVVH and HP were initiated on day 1 and discontinued HP on day 3.

CVVH was stopped on day 7. Normal range: TG 0.29–1.83 mmol/L, CHOL 2.8–5.7 mmol/L, amylase 25–125 IU/L, and lipase 13–60 IU/L. (Reproduced with permission from [286])

the etiology is LPL deficiency, pharmacological therapy is relatively ineffective. In this setting, the role of dietary restriction is central. The pre-pregnancy patient should work closely with the dietician and focus on low fat. Strict adherence to a low-fat diet, usually  $\leq 20$  g/day and sometimes as low as  $\leq 10$  g/day, cuts off the production of chylomicrons [290] and decreases serum TG concentration (Figs. 17.20 and 17.21). However, it paradoxically increases the synthesis of VLDL, leading to enhanced production of TGs by the liver elevating the serum TG levels [292]. Total caloric intake should be adequate, and what little fat is ingested should contain  $\omega$ -3 and  $\omega$ -6 fatty acids [291]. Medium-chain TG-rich foods, such as coconut oil, can be used for cook-

ing, as they are absorbed directly into the portal vein without becoming incorporated into the chylomicron TG. The growing fetus requires essential fatty acids and amino acids to develop and mature vital organs like the brain and lungs. The concern is that a very low-fat diet might lead to a deficiency in essential fatty acids, adversely affecting fetal development, but this is not confirmed.

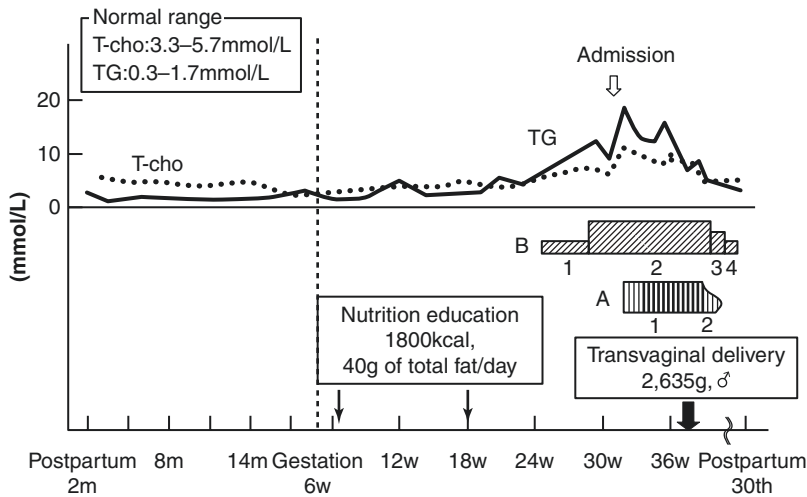
Antioxidant therapy has been used to manage HTG with recurrent AP due to familial LPL deficiency [293]. The antioxidant cocktail ( $\alpha$ -tocopherol,  $\beta$ -carotene, vitamin C, organic selenium, and methionine) significantly reduces the recurrence of AP and could safely be administered during pregnancy. Antioxidants neutralize



**Fig. 17.20** First pregnancy with type V hyperlipidemia was complicated with AP. Treatments were dietary therapy (1), fasting for 11 d; (2), fat-restricted diet including 2.0 g of fat for 6 d; (3), fat-restricted diet including 10.0 g of fat; and (4), fat-restricted diet including 20.0 g of fat

and (A) a protease inhibitor (ulínastatin), (B) antibiotics (piperacillin, sulbactam/cefoperazone), (C) H2-blocker (famotidine), and (D) anticoagulation therapy (heparin) from admission. *T-cho* total cholesterol, *TG* triacylglycerol. (Reproduced with permission from [291])

**Fig. 17.21** The second pregnancy with type V hyperlipidemia of the same patient without AP. Treatments were (A) dietary therapy (1), fat-restricted diet including 20 g of fat daily; (2), fat-restricted diet including 15 g of fat daily and (B)  $\omega$ -3 fatty acids (1), 0.9 g; (2), 2.7 g; (3), 1.8 g; (4), 0.9 g. *T-cho* total cholesterol, *TG* triacylglycerol. (Reproduced with permission from [291])





free radicals resulting from chylomicronemia-related microvascular ischemia, thereby preventing potential damage to pancreatic acinar cells and the resulting AP. Alcohol, oral estrogen therapy, or selective estrogen receptor modulators such as tamoxifen or raloxifene should be discontinued.

### Total Parenteral Nutrition

Weinberg et al. in 1982 confirmed the favorable effect of IV hyperalimentation with nothing by mouth for HTG-induced AP in pregnancy [293]. Avoidance of oral diet and IV administration of 5% dextrose along with insulin (see next section) often dramatically reduces serum TGs [294, 295]. However, IV 5% dextrose does not supply enough calories and cannot be used for the extended duration required for enteric rest. TPN effectively provides the necessary calories and essential amino acids for the growing fetus while controlling the maternal TG concentrations and preventing the induction of AP. TPN with up to 10% of calories of fat does not significantly increase maternal serum TG. This is because of the systemic delivery of lipids which bypasses the liver, where the production of TG-rich lipoproteins occurs. It also enables the supply of other nutritional supplements that the fetus requires. An experienced clinical nutrition support staff should manage parenteral nutrition in pregnancy.

The major complications are related to central venous catheter placement and include pneumothorax, hemorrhage, and rarely death [296]. There has been a trend toward using peripherally inserted central catheters (PICC) because of a lower rate of major complications and relative ease of insertion compared to central venous catheters [296]. PICCs should always be considered, particularly in high-risk populations like pregnant women. However, there is a higher rate of minor complications like thrombophlebitis [278]. PICC insertion is highly operator-dependent, and the lowest complication rates have been seen in the most experienced centers [297].

### L-Thyroxine

Hypothyroidism has a well-established association with hyperlipidemia. In the general population, hypothyroidism is present in 1.4–13% of patients with hyperlipidemia [160], with elevated TG levels in up to 35% of hypothyroid patients [159]. Low circulating free thyroid hormone levels may impair adipose tissue LPL activity. Impaired LDL receptor activity may result in decreased clearance and thus an accumulation of LDL particles. Replacement therapy with L-thyroxine may reverse both defects. In the general population, approximately 50% of those with elevated TSH levels were treated with levothyroxine; 30% of patients with TSH levels >10 mIU/L were not treated. Among patients who received levothyroxine, a considerable proportion (75%) did not require a lipid-lowering agent within 1 year [298]. If this therapy fails, lipid-lowering medications or plasma exchange has been used [226, 299]. In hypothyroidism, glucose uptake in muscle and adipose tissue is also resistant to insulin. The decrease in blood flow in adipose tissue and muscle may be considered part of the pathogenic mechanism of insulin resistance, explaining most of the metabolic defects in these tissues [297]. Hypothyroidism should be searched for in insulin-dependent DM patients because of the synergistic effect of L-thyroxine and insulin.

### Insulin

Insulin activates LPL, an enzyme that accelerates chylomicron degradation into glycerol and FFAs [300]. It also increases its synthesis [136]. Successful management of insulin monotherapy in HTG-induced AP has been demonstrated [226]. Insulin (with the administration of glucose) is safe and effective in treating HTG-induced AP, even in patients without DM [226]. IV insulin may be more effective than subcutaneous insulin in severe cases, given the potential absorption limitations with the subcutaneous route. As required, IV insulin may be given as a continuous infusion starting with 0.1–0.3 U/kg/h with titration.

## Heparin

LPL is a ubiquitous, endothelial-bound lipolytic enzyme. IV heparin uncouples the enzyme from its endothelial anchor, thus stimulating the release of endothelial LPL into circulation [301]. This postheparin lipolytic activity includes predominantly hepatic TG lipase and LPL and other lipases, such as monoglyceride hydrolase and phospholipase, which have lesser hydrolytic activities against a TG substrate. It has been used without insulin to lower HTG [299, 302]. A heparin dose of 10,000 U/day is therapeutic and safe, as evidenced by a normal APTT [45, 299]. Despite the success of IV heparin, in combination with insulin in HTG management, causes an initial rise in circulating LPL levels, followed by increased hepatic degradation [303]. This degradation contributes to further depletion in plasma stores of LPL and may ultimately potentiate the subsequent accumulation of circulating chylomicrons [304]. Another potential hazard is the risk of transformation into hemorrhagic AP with a worsening outcome.

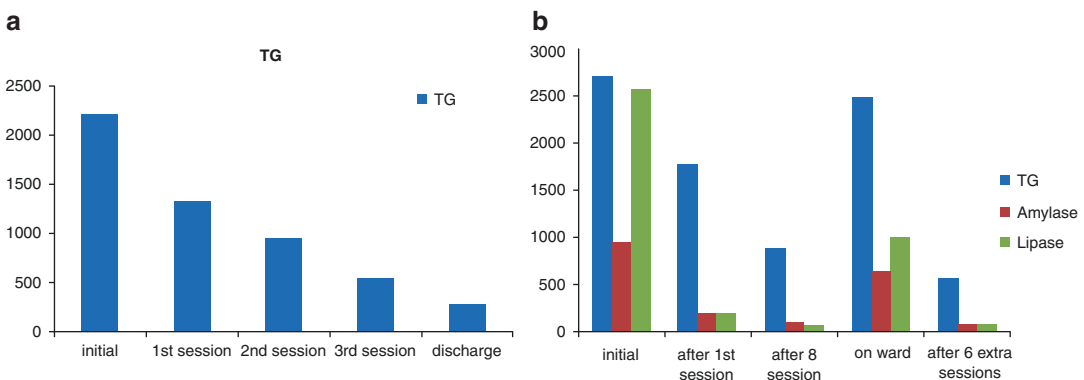
## Plasmapheresis

The first report of plasma apheresis for severe HTG in the general population is from 1978 [305]. Plasmapheresis or lipid apheresis is indicated with [306]:

- Unsuccessful nutritional, lipid-lowering agents or heparin/insulin therapy,
- Serum triglycerides >1000 mg/dL,
- Serum lipase >3× normal upper limit,
- Hypocalcemia,
- Lactic acidosis,
- Worsening inflammation and organ dysfunction.

*Prophylactic plasmapheresis* is a preventive treatment for severe uncontrolled HTG. There is a reduced incidence of HTG-induced AP at 4-week intervals [307]. In one study, 18.1% of patients with HTG-induced AP in pregnancy underwent plasmapheresis with no maternal and fetal complications. TG levels usually rapidly decrease after several sessions of plasmapheresis [43], approximately by 50% after the second session, also depending on the initial values of TG (Fig. 17.22) [43, 308, 309]. Crystalloid solution and albumin are used for plasma exchange with a volume of 40 mL/kg and heparin infusion of 10 U/kg/h for anticoagulation.

Plasmapheresis successfully lowers TG and serum pancreatic enzyme levels [309]. However, in the absence of a comparison with standard treatment (heparin or insulin infusion and lipid-



**Fig. 17.22** (a, b) Lipid profile change with plasmapheresis therapies. TG triglyceride. (Reproduced with permission from [308] under the CC BY 3.0)

lowering agents), the effect of plasmapheresis on lowering the morbidity and length of stay of patients with HTG-induced SAP is uncertain and warrants further investigation. Firm conclusions cannot be made due to a small number of patients. Successful plasmapheresis treatment with dietary intervention is followed by pharmacological therapy that includes fibric acid derivatives,  $\omega$ -3 fatty acids, nicotinic acid derivatives, insulin, or heparin treatment.

*The double-filtration technique* presents major advantages compared to standard plasma exchange [310]. The first filter is a polyvinyl-alcohol hollow fibers membrane, providing pores of 0.2  $\mu$ m diameter in which plasma is separated and then introduced into a second filter with a smaller pore size. This second filter is an ethylene-vinyl-alcohol copolymer membrane, discarding only large-weight molecules such as lipoproteins. In contrast, albumin, IgG, and coagulation proteins are returned to the patient and the whole bloodstream. The loss of low molecular weight molecules such as albumin is reduced, decreasing the required substitution fluid. In addition, IgG and coagulation proteins are saved, thus reducing the major risks of plasma exchange, namely infections and bleeding.

Some authors indicate plasmapheresis as the first treatment with the successful lowering of TG and disappearance of AP symptoms [310]. In addition, this eliminates the need for insulin and heparin therapy, normalizing serum glucose levels.

Swoboda et al. made the first reports of long-term extracorporeal elimination of TG-rich lipoproteins by three modes of treatment (plasma exchange, immunospecific apheresis, and a combination of both treatments) [311, 312]. The loss of immunoglobulins remained acceptable.

Heparin-induced extracorporeal low-density lipoprotein (LDL) precipitation therapy selectively removes LDL cholesterol, fibrinogen, and other lipoproteins from the plasma. It is indicated for lipid management of familial lipidemias or preeclampsia in pregnancy due to beneficial effects of (1) lowering of plasma CRP, (2) increased production of nitric oxide leading to endothelial function improvement, (3) decreased atherogenic LDL oxidation, and (4) inhibition of

expression of endothelial-derived leukocyte adhesion molecules and vascular cell adhesion molecules. The benefit is questionable in HTG AP because it does not lower serum TG levels which cause AP.

### Lipid-Lowering Medications

Plasma exchange, use of lipid-lowering medications, and extracorporeal lipid elimination may effectively control triglyceridemia with or without resulting AP but do not meet the nutritional requirements of the mother and child [311, 313].

#### Fibrates

Fibrates (fibric acid derivatives) include bezafibrate, ciprofibrate, clofibrate, fenofibrate, and gemfibrozil. Fibrates effectively lower TG levels by 40–60% and raise HDL-C levels [314]. The TG-lowering effects of fibrates have been attributed to enhanced catabolism of TG-rich particles and reduced secretion of VLDL [314]. Nicotinic acid lowers TG levels by 30–50% by reducing VLDL secretion, but flushing and gastric upset are prominent side effects [153].  $\Omega$ -3 fatty acids have been proven to lower high TGs (5.5–22.5 mmol/L, 500–2000 mg/dL) by 45% [315]. Fenofibrate 200 mg, niacin 500 mg daily, and  $\omega$ -3 fatty acids are relatively ineffective in patients with primary (genetic) HTG. All fibric acid derivatives are excreted renally and can display a prolonged plasma half-life of several days with severe renal impairment. Since all fibric acid derivatives have a high degree of protein binding (>95%), none are removed by hemodialysis [316]. Gemfibrozil is the most frequently prescribed lipid-lowering agent for patients with renal insufficiency, as it is the least dependent on renal excretion [317]. Gemfibrozil has been reported to cause rhabdomyolysis in patients with compromised renal function. Although most incidences of rhabdomyolysis occur in patients taking both gemfibrozil and HMG-CoA reductase inhibitor [318], rhabdomyolysis induced by

gemfibrozil alone has also been reported [319]. The pathophysiologic mechanism of gemfibrozil toxicity remains unknown, despite its relatively frequent occurrence.

Despite legitimate safety concerns regarding using fibrates, nicotinic acid, and  $\omega$ -3 fatty acids in pregnancy, case reports of patients being prescribed these drugs suggest that they may be safe for both the mother and the fetus [320].

### Statins

Epidemiological data suggest that statins are not major teratogens but are currently contraindicated in pregnancy (FDA class X). The percentages of normal outcomes (85%), congenital abnormalities (4%), spontaneous abortions (8%), fetal deaths/stillbirths (1%), and miscellaneous adverse outcomes (2%) are not higher than those expected in the general population [321, 322]. The actual risk for an exposed pregnancy seems small and does not warrant termination of pregnancy. Nevertheless, avoiding using these drugs in patients planning a pregnancy is still advisable to reduce the risks [323]. There are also cases of statin-induced AP in the general population (see Sect. 17.3). There are no recommendations for hyperlipidemic AP in pregnancy where the benefits could outweigh the risks, including the short duration of statin therapy.

#### 17.7.1.6 Primary Hyperparathyroidism

Medical therapy in pregnancy for symptomatic PHPT has been discouraged due to the safety issues of drug therapy and the suboptimal control of serum calcium, leading to a high fetal loss rate [69]. However, some groups of patients diagnosed in the third trimester may be managed medically, postponing the operation until after delivery:

- Symptom-free patients,
- No radiologically identifiable parathyroid adenoma,
- Mild hypercalcemia,
- Significant hypercalcemia who are not surgical candidates.

Medical therapy primarily involves stabilizing the patient with hydration, limiting calcium intake, and correcting electrolyte imbalance. Early treatment of urinary tract infections and avoiding medications known to cause elevations in serum calcium, such as vitamin D, vitamin A, aminophylline, and thiazide diuretics, are essential therapeutic measures. Serum calcium should be determined regularly.

High-dose *magnesium sulfate infusion* might be a therapeutic alternative for PHPT in pregnancy [71, 84, 89]. A compensatory increase in serum vitamin D-1,25 in response to the decrease in the PTH level caused by magnesium can increase calcium absorption from the gastrointestinal tract. Therefore, for some patients, because of persistent hypercalcemia, magnesium sulfate might not be a viable treatment option for PHPT during pregnancy [71].

When magnesium proves ineffective, other agents such as phosphate-of-soda enemas, oral phosphates phosphate (inorganic phosphorus in doses of 1.5–2.5 g/day), and loop diuretics have been used with varied success [62, 70, 84, 104]. Side effects of *oral phosphate* therapy include nausea, vomiting, and hypokalemia. This can be avoided by decreasing the dose of medication.

Calcitonin is administered if the patient with the indication for operative treatment chooses medical therapy for PHPT. It is considered the safest conservative treatment option in pregnant patients with hypercalcemia [69]. The safety probably results from its negligible passage through the placenta [104, 324]. The choice of this agent was also supported by suggested but not fully supported beneficial effects of calcitonin in the management of AP observed in non-pregnant patients. Most recommend maintaining total plasma calcium  $<3.0$  mmol/L [323] to limit the risk of serious complications. Exceeding this level is considered an indication of calcitonin administration. Interestingly, although calcitonin treatment may be associated with developing tachyphylaxis [325], the only tendency to tachyphylaxis was observed in the third trimester. It disappeared after the introduction of oral phosphates. This fact might be explained by administering this agent only if plasma calcium levels exceed the established threshold. Moreover, there

were no nausea, vomiting, diarrhea, flushing, injection site reactions, or other side effects associated with calcitonin treatment [325]. The benefits of combined administration of calcitonin and cinacalcet in pregnancy and puerperium have been shown [326]. Transient mild hypocalcemia probably resulted from increased calcium levels in fetal plasma, inhibiting parathyroid PTH synthesis and release during the pregnancy [104, 324]. Interestingly, neonatal hypocalcemia was absent in the patient's subsequent pregnancy after parathyroidectomy. This supports the recommendations that surgery should be considered the treatment of choice in young PHPT pregnant women or desiring pregnancy [75, 191].

In the past, *mithramycin* was used but is currently contraindicated secondary to teratogenic effects [79].

*Corticosteroids* have also been used to decrease the absorption by the gastrointestinal tract but have shown a minimal effect when hypercalcemia is secondary to PHPT [79].

#### 17.7.1.7 Acute Fatty Liver of Pregnancy

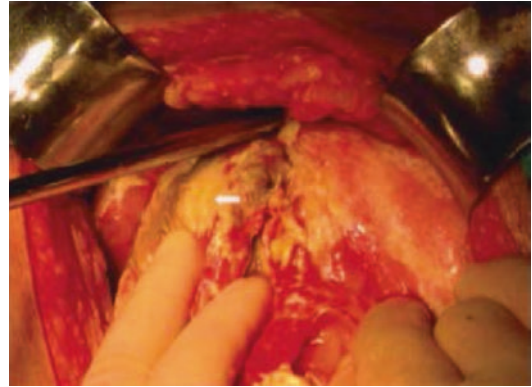
See Sect. 16.2.4.2.

### 17.7.2 Surgical Treatment

Surgical treatment has two aspects: operative intervention for the AP itself and management of associated local (biliary tract disease, pancreatic tumor) or distant (PHPT, HTG, etc.) causes of the AP during an attack or once the acute inflammation subsides.

Surgery for necrotizing AP in pregnancy should be delayed as long as possible [23]. Remission is achieved in most patients (78.9%) with conservative treatment. Therefore, the indications for surgery and antibiotics are [23, 274–276, 287] as follows:

- Pancreatic necrosis and infection (3–4 weeks after the onset of symptoms),
- Large intra-abdominal exudates,
- Clinical deterioration.



**Fig. 17.23** Prominent pus coating over the omentum, intestine, and colon, peripancreatic fatty necrosis, and excessive solid mass of swollen inflamed pancreas. An area of impending perforation (arrow) is over the transverse colon. (Reproduced with permission from [245])

Percutaneous, endoscopic, or minimally invasive surgical techniques are getting wider acceptance. The decompression and percutaneous drainage help to avoid or delay surgery in most patients with SAP [23, 276]. For patients with pancreatic abscesses, drainage is recommended [275]. Necrosectomy (Fig. 17.23) should be performed as late as possible, and it can also be performed during the CS through median laparotomy.

#### 17.7.2.1 Pancreatic Pseudocysts

Limited information is available to guide the management of pancreatic pseudocysts in pregnancy. Many reports during pregnancy have limited value due to a lack of US measurements. In the general population, the recommended management is to observe (1) asymptomatic pseudocysts, (2) those present for <6 weeks, and (3) pseudocysts <5 cm in diameter, as these have a 30–40% rate of spontaneous resolution. Although it is recommended that uncomplicated pseudocysts should be surgically managed during the postpartum period [327, 328], the pseudocyst might rupture because of the decreasing space within the abdominal cavity due to the growing uterus or later during delivery [329]. Seventy-six percent were treated postpartum with definitive surgical treatment after various antenatal “holding” maneuvers [56, 330]. When the pseudocyst is infected, located greater than



1 cm from the bowel, or has a cyst wall insufficiently thick to permit anastomosis, percutaneous drainage should be considered despite a recurrence rate of 20–70% [331, 332] and the potential risks of infection and fistulation [332]. An indwelling transgastric or transduodenal pig-tail catheter may be placed, or a more permanent internal fistula may be created by cautery between the cyst and the adjacent viscus. This last procedure, while reportedly effective, carries a significant risk of bleeding and depends on the skill of the endoscopist. Endoscopic transpapillary stenting is another alternative for patients with a partial pancreatic duct disruption and a communicating pseudocyst.

Surgical internal drainage is preferred for:

- Symptomatic pseudocysts,
- Pseudocysts >5 cm in diameter,
- Those present for >6 weeks.

These have a 3% chance of resolution and a 57% risk of rupture, infection, bleeding, or obstruction [331]. Internal drainage can be accomplished by anastomosis to the duodenum, a Roux-en-Y limb of the jejunum, or the posterior wall of the stomach.

Table 17.6 compiled the available information on the presentation, etiology, management, and outcomes of pancreatic pseudocysts since 1980 [57]. Pancreatic pseudocysts complicate 6.9% of AP. Most women are primiparous. Hyperlipidemia and idiopathic PA are the most common causes. Gallstones, the most common cause of AP during pregnancy [13], account for 14%.

The natural history of pancreatic pseudocysts is similar to nonpregnant patients because pseudocysts <5 cm shrink or resolve while those >5 cm remain the same size or enlarge. In three cases, the intervention was performed antepartum: two patients underwent percutaneous drainage, and one was stented endoscopically. Percutaneous drainage of pseudocysts >6 cm failed [53, 332]. Sometimes

different drainage interventions are needed to successfully treat pseudocysts >6 cm [330].

### 17.7.2.2 Pancreatic Tumors

Mucinous cystic neoplasms are considered premalignant lesions, and resection is recommended. Cystic neoplasms are even less common than pancreatic pseudocysts but can occur during pregnancy and may mimic inflammatory fluid collections. Factors differentiating inflammatory from neoplastic fluid collections include serum amylase level, which is elevated in 50–75% of pseudocysts [332] and 5% of pancreatic neoplasms [332]; cyst amylase level, which is normal in neoplasm and elevated in inflammatory fluid collections; US demonstrating multiple cysts or internal septa suggest neoplasm rather than inflammation [332]; and history of AP or antecedent factors suggesting inflammatory causes such as gallstones, hyperlipidemia, or alcoholism.

### 17.7.2.3 Primary Hyperparathyroidism

PHPT in pregnancy represents a significant risk for maternal and fetal complications that cannot be predicted by the duration of symptoms or serum calcium levels. Indications for parathyroidectomy, regardless of the trimester of pregnancy, are [112] as follows:

- Persistent symptoms,
- Serum Ca >11 mg/dL,
- Acute pancreatitis.

In 1947, Petit and Clark carried out the first parathyroidectomy during pregnancy [335]. Successful surgical management of PHPT eliminates the risk of PHPT deterioration postpartum and the risk of neonatal tetany. The second trimester is recommended as the optimum time for surgery after all the fetal systems have developed. The fetus has time to recover its parathyroids, reducing the risk of neonatal tetany. Previously surgery during the third trimester has been reported to increase

**Table 17.6** Characteristics of pancreatic pseudocysts in pregnancy [57, 251, 257, 333, 334]

| Author    | Age/gravida, para/EGA                   | EGA when cyst was found  | Size and location           | Etiology                       | History of cyst                                                                                                              | Management                                                                                                | Delivery   | Morbidity and mortality                                       |
|-----------|-----------------------------------------|--------------------------|-----------------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|------------|---------------------------------------------------------------|
| Nies      | 26 years old/para 0/34 weeks            | PP                       | 6 cm, tail                  | Lipid                          | Remained the same size                                                                                                       | Conservative                                                                                              | Vaginal PT | Pleural effusion versus pneumonia; ICU                        |
| Glueck    | gravida 1, para 0/39 weeks              | PP                       | N/A                         | Lipid                          | N/A                                                                                                                          | Conservative                                                                                              | Vaginal T  | Ruptured cyst, shock, ICU                                     |
| Chen      | 28 years old/gravida 2, para 1/31 weeks | 31 weeks                 | 4 cm, tail                  | Lipid                          | Shrunk to 2 cm spontaneously                                                                                                 | Conservative                                                                                              | N/A        | None                                                          |
| Bar-David | 28 years old/gravida 1, para 0/17 weeks | 29 weeks                 | N/A                         | Lipid                          | Infected pancreatic pseudocyst noted at 29 weeks, disappeared by 37 weeks                                                    | Conservative                                                                                              | Vaginal T  | Septic shock, pneumonia with mechanical ventilation, TPN, ICU |
| Stowell   | 37 years old/gravida 3, para 2/31 weeks | 31 weeks                 | 5 cm, head; 8 cm, tail      | Alcohol                        | Cyst in head resolved; tail cyst remained the same size                                                                      | Conservative; PP cystogastrostomy                                                                         | Vaginal T  | TPN for 5 weeks; FGR                                          |
| Ryan      | 35 years old/6 weeks                    | Present before pregnancy | 6 cm, tail                  | Idiopathic (alcohol?)          | Grew to 7 cm; shrunk to 2 cm after stent; grew to 4 cm when stent fell out; stent replaced and cyst stable until 2 months PP | Cystogastric stent placed by ERCP at 17 weeks; transpapillary stent placed at 35 weeks; PP pancreatectomy | Vaginal T  | None                                                          |
| Beattie   | 20 years old/gravida 1, para 0/24 weeks | 27 weeks                 | 13 cm, posterior to stomach | Anatomic                       | 1 L of fluid aspirated, then daily aspirations                                                                               | Percutaneous drainage at 24 weeks; PP hepatico-jejunostomy                                                | C/S PT     | Cyst collapsed around drain                                   |
| Eddy      | 24 years old/gravida 3, para 0/26 weeks | 26 weeks                 | 6 cm, tail                  | GS                             | Grew to 15 cm                                                                                                                | Conservative; PP pancreatectomy                                                                           | C/S T      | TPN for 3 weeks; splenectomy                                  |
| Swisher   | N/A                                     | N/A                      | 6 cm                        | Non-GS (alcohol or idiopathic) | N/A                                                                                                                          | Percutaneous drainage                                                                                     | N/A        | N/A                                                           |

(continued)

**Table 17.6** (continued)

| Author   | Age/gravida, para/EGA                       | EGA when cyst was found | Size and location | Etiology             | History of cyst   | Management                    | Delivery           | Morbidity and mortality                                                       |
|----------|---------------------------------------------|-------------------------|-------------------|----------------------|-------------------|-------------------------------|--------------------|-------------------------------------------------------------------------------|
| Hess     | 25 years old/<br>gravida 1, para 0/31 weeks | PP                      | N/A               | Hyperparathyroidism  | N/A               | Conservative                  | Induced vaginal PT | Initial mental status changes, hypocalcemia after neck surgery, renal failure |
| Qin      | ?/G1P0/32                                   | 33 weeks                | –                 | Lipid                | None              | Conservative                  | Vaginal PT         | None                                                                          |
| Gyokeres | 28/G1P0/21                                  | 14 weeks                | 8 × 7.5 cm, body  | Idiopathic           | No change in size | Endoscopic cystogastrostomy   | C/S PT             | None                                                                          |
| Bansal   | 26/G?P?/13                                  | 13 weeks                | 14 × 7 cm, body   | Gallstones           | None              | Laparoscopic cystogastrostomy | Vaginal T          | None                                                                          |
| Bernica  | 31/G5/19                                    | 19 weeks                | 20 × 13 cm, body  | Idiopathic (lipid ?) | None              | Endoscopic cystogastrostomy   | C/S T              | None                                                                          |

*G* gravity, *P* parity, *EGA* estimated gestational age, *N/A* information not available, *GS* gallstone pancreatitis, *PP* postpartum, *C/S* cesarean section, *T* term, *PT* preterm, *TPN* total parenteral nutrition, *ICU* transfer to intensive care unit, *FGR* fetal growth restriction

the risk for preterm labor [112] and other severe complications. However, these complications could be due to the longstanding hypercalcemic status of both the mother and the fetus [65, 112]. Others do not mention any increased risk of maternal or neonatal complications [336–338].

Surgical treatment should be considered early. A minimally invasive approach preceded by preoperative localization of the parathyroid adenoma with US and intraoperative monitoring with serial PTH measurements mitigates the risk to the mother and fetus. It is recommended to locate and identify the parathyroid adenoma before proceeding with any surgical intervention; however, if the adenoma cannot be located with imaging, neck explorations have a 95% chance of cure [69]. Preoperative tumor localization in pregnancy using Tc-99m-sestamibi scanning has been successful [75]. Advantages include avoidance of unnecessary surgical exploration, decreased complication rates, and shortened anesthesia time. The low doses and short half-life minimize fetal radiation exposure. Serial intraoperative PTH measurements are easily obtained, confirm complete adenoma removal, and exclude multiglandular disease [191, 202].

With the parathyroid gland in the superior mediastinum, a cervical approach with or without sternotomy could be considered. The need to remove a parathyroid gland in the mediastinum is infrequent [332]. Although the removal of an ectopic parathyroid gland through a cervical incision may be successful in many patients, a median sternotomy is often required. This procedure has the potential to cause more morbidity and is associated with up to 12–21% incidence of chest complications [339, 340]. Video-assisted thoracoscopic surgical (VATS) techniques have decreased the need for sternotomy to remove ectopic glands [334]. Also, radio-guided (questionable during pregnancy) parathyroidectomy via VATS, combined with intraoperative PTH assay, can be performed [341]. Compared to median sternotomy, VATS offers all the benefits of surgical resection plus the potential of a marked decrease in general morbidity and hospital stay [342].

In patients undergoing surgical treatment, transient hypocalcemia may occur after surgery. Serum calcium should be checked every 6 h, and if the patient develops hypocalcemic symptoms, IV calcium in the form of calcium gluconate, 10–20 mL of a 10% solution, should be given over 5–10 min. Intermittent infusions in 5% dextrose or isotonic saline and infused continuously at 1 mg/kg/h. Post-surgical hypocalcemia may be profound in patients with bone disease, and aggressive treatment is needed. These patients may need vitamin D supplementation (calcitriol 0.25–0.5 µg/day) for a few days before the operative intervention.

The effectiveness of the surgical intervention in preventing fetal and neonatal complications indicates that successfully treated PHPT cannot be regarded as a contraindication for consecutive pregnancies. Approximately 67% were diagnosed during the third trimester [230]. More than half underwent neck exploration after delivery. Half of the patients diagnosed before the third trimester underwent surgery during the second trimester and another half in the puerperium [230].

#### 17.7.2.4 Biliary

Biliary AP recurrence is observed in 50% after conservative treatment [343]. The early readmission rate is twice of nonpregnant women. Half of these readmissions are due to adverse events related to AP, including pseudocysts, drainage procedures, and recurrent AP [273].

### 17.7.3 Therapeutic Delivery

Therapeutic delivery is indicated to cure the pregnancy-induced AP of any cause, resistant to conservative or surgical treatment of AP. Obstetric indications are not part of the therapeutic delivery. An additional beneficial effect of therapeutic delivery is that medications contraindicated during pregnancy can be used. The mode of delivery is determined by obstetric factors [344].

Stimulating fetal lung maturation with corticosteroids in the critical period for delivery is essential. In experimental animals, administration of 17

beta-estradiol accelerates fetal lung maturation and stimulates surfactant production: The hormone increases the amount of surfactant in fetal lung lavage, increases the rate of phosphatidylcholine synthesis, depletes fetal lung glycogen, and accelerates morphological maturation of the fetal lung. Estrogens and glucocorticoids stimulate fetal lung choline phosphate-cytidylyltransferase, a critical enzyme in regulating phosphatidylcholine synthesis. Estrogen increases the catalytic activity rather than the amount of choline phosphate-cytidylyltransferase. This action of estrogen is mediated by phospholipids [345].

### 17.7.3.1 Hyperlipidemia/ Dyslipidemia

Because pregnancy might lead to the exacerbation of HTG in patients with familial hyperlipidemia, therapeutic delivery in resistant cases is advocated. It is estimated to lower lipid levels by 15–20% within 24 h and return them to prepregnant levels by 6 weeks postpartum [141, 311, 346]. Both cholesterol and TG concentrations decreased significantly within 24 h of delivery [347], which was reflected in all lipoproteins. However, the morbidity from AP does not always fall proportionally. Rapid improvement [347] and worsening of hyperlipidemic AP after delivery [59] have both been described, and AP can progress to maternal death [206].

While TG levels continue to decrease rapidly, returning to nonpregnant levels during the puerperium, cholesterol in low-density lipoprotein remains elevated for at least 6–7 weeks postpartum [348]. Early delivery may allow more aggressive treatment of the mother, including using lipid-lowering agents such as statins, contraindicated in pregnancy (FDA class X). Delivery also lowers intra-abdominal pressure, makes it easier to resuscitate the mother, and may prevent fetal distress if AP causes rapid maternal deterioration. Also, it is easier to proceed with enteral nutrition.

Failure of  $\geq 2$  organs in SAP has a high incidence of fetal loss, so early therapeutic delivery is advocated.

### 17.7.3.2 Gallstones and Unknown Causes

In AP, due to gallstones or unknown causes, the rapid resolution has been described after intra-uterine fetal death [19] and after vaginal delivery with live birth [349]. Fortunately, gallstone AP is successfully treated with endoscopic, surgical, or combined procedures, and delivery is indicated only for obstetric indications (most commonly fetal distress).

### 17.7.3.3 Preeclampsia/Eclampsia

Preeclampsia is a severe form of pregnancy-induced hypertension and can lead to epileptic-like grand mal convulsions (eclampsia) in 0.1% of pregnancies. A cerebral vascular accident is the most common cause of death. The disease has no known cause and can only be cured by delivery.

### 17.7.3.4 Acute Fatty Liver of Pregnancy

See Sect. 16.2.4.2.

### 17.7.3.5 HELLP Syndrome

AP caused by HELLP syndrome can only be cured by therapeutic delivery [350].

## 17.7.4 Obstetric Management

### 17.7.4.1 Mode of Delivery

Spontaneous vaginal delivery is the preferred delivery route in women with AP because CS may cause penetration of the accumulated fluids resulting in contamination, intraperitoneal leakage, and sepsis [351]. Also, hypotension during CS can exacerbate AP due to impaired pancreatic blood supply and hypoxia [352]. However, when pancreatic pseudocysts are present, CS is recommended to minimize the risk of rupture during Valsalva efforts during vaginal delivery [58, 351]. Others state that the mode of delivery in patients with associated pancreatic pseudocysts should be determined on a case-by-case basis [57] because vaginal delivery was achieved in 69% of published cases [56, 330, 353]. In a series with AFLP-induced AP, CS was performed in 67%



[203]. With some exceptions [57], morbidity (Table 17.6) resulted from AP or its underlying cause rather than the pancreatic pseudocyst. Indications for termination of pregnancy include [102] the following:

- Signs of miscarriage or premature birth,
- Fetal distress or intrauterine deaths,
- If the fetus can survive, choose CS timely; if the fetus is dead, make labor induction.

## 17.8 Prognosis

### 17.8.1 General Considerations

#### 17.8.1.1 Maternal Outcome

Improvements in diagnostic and therapeutic (surgical, endoscopic, and obstetric) modalities and ICU care in the pregnant population improve maternal outcomes. In the 1970s, reported maternal mortality was up to 37%, while in nonpregnant patients from that period under 50 years of age, it ranged from 3.1 to 6.6% [14, 19, 346, 354–356]. Maternal mortality through previous decades varied from 20 to 50% and most occurred during the third trimester [13, 14, 18]. Maternal mortality during the 20 years before the millennium in Japan was 7.5%, without maternal death since 1985 [357, 358]. Recent reports claim overall maternal mortality of <1% [25, 29, 40, 102], with several studies without maternal deaths [13, 23, 32, 53].

The maternal outcome depends on several factors. Some are the same as in the general population:

- Pancreatitis severity,
- Pancreatitis etiology,
- Trimester,
- Maternal age,
- Maternal comorbidities.

These prognostic factors are interrelated. Most importantly, the severity of AP during pregnancy depends on the cause of AP.

Non-gallstone AP had worse maternal and fetal outcomes compared to simple gallstone AP.

Better maternal and fetal outcomes result from increased cholecystectomy rate in pregnant women who developed AP or symptomatic cholelithiasis/cholecystitis, especially in early trimesters [25, 29, 32]. This supports the high relapse of biliary colic and its complications during pregnancy [359]. Also, in earlier studies, the recurrent AP risks were 50–72% during the same pregnancy [23, 53]. Traumatic, hyperlipidemic, and alcohol-induced AP has particularly poor outcomes [25]. Post-ERCP AP does not adversely affect pregnancy-related outcomes [29].

More than 90% developed AP in the last two trimesters, and almost all SAP cases were in the third trimester [20, 29, 31]. The large uterus limits gallbladder motility and produces pancreatic ischemic injury. Estrogen-related increases in serum TG levels produce hyperviscosity, leading to ischemia and acidosis in pancreatic capillaries [360, 361]. Changes in bile composition secondary to high estrogen levels in the last trimester may induce the formation of gallstones and sludge [360], which are the leading causes of AP.

Aging is associated with increased AP severity characterized by augmented and prolonged pancreatic inflammation with multiple extrapancreatic sequels, including thrombosis [362]. Serious maternal pulmonary complications are often associated with AP. The destruction of pulmonary surfactant by degradation of lecithin and increased serum PLA2 results in increased lung capillary permeability and elevated surface tension. This leads to pulmonary edema, causing acute respiratory insufficiency [363]. It is unknown whether this mechanism increases perinatal morbidity and mortality.

### 17.8.1.2 Fetal Outcome

Previously, perinatal mortality of 50% [14] resulted from neonatal deaths after preterm delivery. Mortality rates improved in the last 20 years due to improved neonatal ICU care and better supportive treatment of AP [13]. Outcomes for the mother and fetus in 1970 were similar to 21% maternal and 20% fetal mortality rates [346]. From the 1990s, perinatal mortality rates improved, with up to 74% of healthy term deliveries and a 10.5–17% fetal mortality rate [13, 142]. Even preterm babies delivered by CS could be saved due to improvements in perinatal care. The recent perinatal mortality rate is 0.57–4.7% [23, 25, 364] and 19% of preterm labor [23]. The fetal outcome depends on the following:

- Trimester,
- The severity of AP,
- The cause of AP,
- Organ failure.

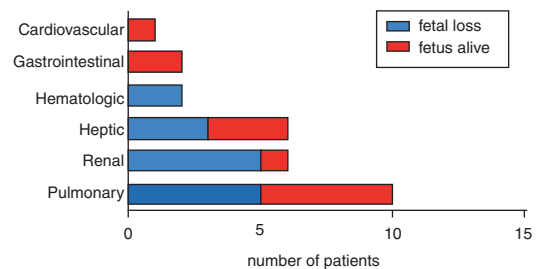
Most publications do not distinguish between the various causes and severity of AP. In a Turkish study, nearly half of the patients had SAP, and in contrast to the MAP group, where 57% of the deliveries occurred beyond 37 weeks, in the SAP group, 83% of deliveries occurred prematurely. This finding is consistent with the study of Geng et al., with a fetal loss of 33% and a preterm delivery rate of 39% among SAP patients [32]. Also, the term delivery rate in the MAP group was significantly higher than in the SAP group, while the fetal loss was different between MAP and SAP [20]. Late abortion (70%) and preterm infants (30%) constituted the fetal loss in the MAP group, while fetal death and stillbirth were the main fetal loss components (83.3%) in the SAP group [20]. Considering these findings, prematurity seems to be related to the severity of AP. Some studies did not find a statistical difference between fetal death and preterm births for biliary and HTG-induced AP [142]. On the other hand, MAP was a more common (77%) variant in

biliary AP [142]. For placental abruption/uteroplacental apoplexy, see Sect. 4.7.2.

Patients who developed AP in the first trimester have the lowest probability of reaching term pregnancy (60%) and the highest risk of fetal loss (20%) [24, 29]. Preterm labor may occur in up to 60% of patients with AP in late pregnancy; therefore, gestational age is a primary determinant of perinatal outcome.

The fetal outcome is organ failure dependent. Two or more organ systems involved carry the highest risk of fetal loss [32]. Figure 17.24 shows the distribution of the failure of organs. The lung is the most vulnerable organ; the kidney and the liver are also easily affected. Renal and coagulation disorders denoted poor prognosis, whereas gastrointestinal and cardiovascular dysfunctions were not common in SAP.

The mechanisms of demise also include placental abruption and profound metabolic disturbance, including acidosis. Altered maternal acid-base status can adversely affect fetal acid-base status. Acute fetal hypoxia activates some compensatory mechanisms for the redistribution of blood that enable the fetus to achieve constancy of oxygen consumption in the fetal cerebral circulation and the fetal myocardium. Redistribution of blood to vital organs allows fetal survival for a moderately long period of limited oxygen supply. However, these responses are no longer maintained during more severe or sustained hypoxemia, and decompensation with fetal tissue damage and even fetal death may occur [51, 364].



**Fig. 17.24** Distribution of organ failure during acute pancreatitis in pregnancy. (Reproduced with permission from [32])

AP complicated by DIC usually occurs in the third trimester and is particularly associated with poor fetal outcomes [29]. Hepatobiliary diseases can result in maternal and fetal physiological dysfunction, leading to adverse pregnancy outcomes, such as prematurity and low birth weight [365]. Thus, it is imperative to identify hepatobiliary disease early during pregnancy to intervene appropriately as early as possible.

## 17.8.2 Primary Hyperparathyroidism

Postoperative (parathyroidectomy) pregnancy outcomes showed a four- to fivefold decrease in maternal/fetal complication rates [75]; therefore, surgical therapy is recommended.

### 17.8.2.1 Maternal Outcome

Untreated severe PHPT during pregnancy without AP results in maternal complication rates as high as 67% [69]. Clinically significant complications related to PHPT were as high as 25% in the medically managed patients compared to 12.5% in the surgically managed group [75]. Increased risk for maternal complications apart from AP includes visceral calcification, particularly nephrolithiasis/nephrocalcinosis (24–36%), generalized weakness, hyperemesis, muscle cramps, and bone resorption (subperiosteal resorption (especially on the radial aspect of the middle phalanges of the hand), preeclampsia/eclampsia, and lethargy/psychiatric problems (irritability, depression, and marked insomnia)) [69, 79]. If the mother is treated medically to term (or if spontaneous or elective abortion occurs), the mother should be monitored for *hypercalcemic crisis* postpartum. Crisis can present in the early puerperium due to the sudden interruption of the transplacental shunting of calcium from the mother to the fetus [64, 69]. It is a life-threatening complication of PHPT during pregnancy, seen with serum calcium levels >14 mg/dL, and is characterized by nausea, vomiting, tremors, dehydration, and mental status changes, which can progress to uremia, coma, and even death [79].

Up to 1998, maternal mortality from PHPT-induced AP was 15% [91] without further mortality [230]. Mortality seems to be related to delayed resection of parathyroid tumors [91]. Hypercalcemic crisis can occur if emergent CS is performed during pancreatic necrosectomy and drainage.

### 17.8.2.2 Fetal Outcome

Untreated severe PHPT during pregnancy results in fetal complication rates as high as 83% and neonatal complication rates as high as 53% (30% represent neonatal deaths) [69]. The complications include intrauterine/neonatal demise, second-trimester loss, and generalized tetany after delivery [79]. The patients with calcium levels of 10.7 mg/dL were associated with pregnancy loss, but most pregnancies continued to term. Calcium >11.4 mg/dL was associated with 72% of fetal loss [366]. From 1930 to 1990, 70 patients were treated medically and 39 surgically during pregnancy [62]. Of those treated medically, 53% of neonates had complications, and 16% died. In contrast, in the group managed surgically, 12.5% of neonates had a complication, and only 2.5% died. Therefore, the fetal mortality rate with PHPT without AP can be reduced four times with operative treatment [62, 69, 367]. In addition, there are studies without maternal or fetal complications after surgery [65].

Neonatal hypocalcemia with tetany is usually transient due to the suppression of fetal parathyroid glands resulting from maternal–fetal hypercalcemia. It may be more prolonged in mature infants or infants with birth asphyxia. PHPT results in high concentrations of fetal serum calcium that act to suppress the parathyroid glands. Fetal calcitonin concentrations are high to encourage bone mineralization. At birth, however, the neonate is suddenly deprived of this source of calcium. It is incapable of mobilizing calcium from the bone owing to the low concentrations of parathyroid hormone and high concentrations of calcitonin. *Acute neonatal hypocalcemia*, first described by Friderichsen in 1939 [368], results in neonatal tetany and convulsions, usually at 5–14 days of age. If the

infant is breastfed, tetany can be delayed by 1 month or more [332, 369].

In 13 patients with PHPT with AP up to 1998, fetal mortality was 23% [91]. Mortality seems to be related to delayed resection of parathyroid tumors [91].

### 17.8.3 Acute Fatty Liver of Pregnancy

See Sect. 16.2.4.2.

### 17.8.4 Hypertriglyceridemia

#### 17.8.4.1 Maternal Outcome

The severity of HTG-induced AP or its complications does not correlate with TG level [370], similar to the general population. When the entire dyslipidemic group in the general population is analyzed, the indices of SAP and complications are predominant in the HTG group, irrespective of the grade [371]. One of the explanations is that HTG is often associated with additional negative prognostic factors such as DM (the prevalence of DM in dyslipidemic AP in the general population is around 30% [371]), obesity, and alcohol consumption. In one of the largest studies, HTG-induced AP had a severe form in 77% of patients, biliary AP in 44%, and alcohol-induced AP in 0% [20]. In another study, isolated HTG-induced AP was the cause of 50% of SAP in pregnancy [32]. Therefore, HTG-induced AP in pregnancy is a severe complication associated with a significant risk of death for both the mother (21%) and the fetus (20%) [346]. However, no maternal death was reported in 15 cases of gestational hyperlipidemic AP [35, 295]. Although severity and complication rates with HTG-induced AP have been reported as higher than AP from other etiologies, mortality rates were not different. In the general population, patients with HTG-induced AP had significantly more prior episodes of AP than with biliary AP and more complications, such as pancreatic necrosis, abscess formation, sepsis, or renal insufficiency, without mortality in both groups [372]. A recent study showed a lower Ranson score with HTG-induced AP compared to biliary AP. Also, the mortality was nil in the

HTG-induced AP group compared to 22% in the biliary AP group. A possible explanation is an early diagnosis of HTG with immediate therapeutic lowering of its serum values.

#### 17.8.4.2 Fetal Outcome

Studies show the highest fetal mortality rate in HTG-induced AP. In some studies, almost all fetal losses were due to HTG-induced AP in its severe form, resulting in 38.9% preterm delivery and 33% fetal loss rate [32].

HTG is often part of metabolic syndrome, including DM. Maternal DM leads to a higher fetal risk of developing impaired glucose tolerance and obesity during adulthood. Maternal hyperinsulinemia and transient hyperglycemia impair pancreatic endocrine development in the control offspring and induce multiple metabolic alterations in early postnatal life. The relatively smaller  $\beta$ -cell mass/area and  $\beta$ -cell proliferation in these control offspring suggest cell-autonomous epigenetic mechanisms in regulating islet growth and development [373]. Fetal development in a diabetic environment is characterized by increased insulin secretion due to overstimulation and possibly resulting in exhaustion of the fetal pancreatic  $\beta$ -cells. The risk for DM is significantly higher when the mother, rather than the father, has non-insulin-dependent DM [374]. Furthermore, 35% of patients with gestational DM are offspring of diabetic mothers compared to 5% of normoglycemic mothers, and gestational DM occurs more frequently in the offspring of diabetic mothers (35%) than in the offspring of diabetic fathers (7%) [375]. The most common human structural birth defects associated with pregestational DM are congenital heart defects and central nervous system defects. However, DM can induce birth defects in any other fetal organ. In general, the rate of birth defects increases linearly with the degree of maternal hyperglycemia, a major factor that mediates the teratogenicity of PGD. In addition, because many of the components of metabolic syndrome result in increased low-grade systemic inflammation [376], increased stimulation of the inflammation pathway conferred from the mother with metabolic aberrations to the fetus might explain the increased risk of medically indicated

preterm births in women with metabolic syndrome in early pregnancy. Therefore, it is sometimes difficult to “accuse” only a single event, such as AP, for adverse fetal outcomes.

### 17.8.5 Biliary

Maternal mortality is similar with conservative and surgical treatments, but fetal mortality is significantly higher in patients who did not rapidly benefit from the supportive treatment [364]. In nonresponders and those with acute cholangitis during follow-up, ERCP, ES, biliary stent placement, or cholecystectomy should be performed. Current maternal mortality is 0% [377].

### 17.8.6 Medications

The prognosis of drug-induced AP in the general population is excellent. In one report of 22 cases, 19 were associated with interstitial AP, none of the patients with pancreatic necrosis, none over 33% of the pancreas involved, and none died [173]. Mortality has also been rare in other reviews, although reports of a few deaths related to drug-induced AP exist.

### 17.8.7 Alcohol Abuse

#### 17.8.7.1 Maternal Outcome

Patients with alcohol-induced AP were more likely to have a recurrence of AP during pregnancy (75% vs. 29%) from AP of other causes [25]. Pseudocysts were almost exclusively associated with non-gallstone AP [25].

#### 17.8.7.2 Fetal Outcome

Patients with alcohol-induced AP were more likely to have a preterm delivery (67% vs. 26%) than in cases where alcohol was not a factor [25].

### 17.8.8 Preeclampsia/Eclampsia

All maternal deaths and intrauterine fetal demise were published before 1973 [93]. One recent case

with maternal death resulted from rapid deterioration. Unfortunately, serum/urine amylase and lipase were not taken during the disease, and also, the authors did not perform the abdominal CT [378].

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## Abstract

Intestinal obstruction is one of the five most common causes of nonobstetric acute abdominal conditions during pregnancy. A wide variety of causes can present during pregnancy, as in the nonpregnant population. Some conditions are significantly more common in pregnancy than in the nonpregnant population. These include cecal and sigmoid volvulus and intussusception (compared to the female population of the same age range) due to the growing uterus displacing surrounding organs and increased intra-abdominal pressure. The presentation is similar or the same for any underlying cause of intestinal obstruction and depends on obstruction level and severity. Clinicians avoid using plain abdominal X-ray, which is commonly diagnostic and adds to earlier diagnosis, influencing maternal and fetal prognosis. Conservative therapy is rarely successful except for adhesive small bowel obstruction. Still, it is less successful than in the general population due to partially fixed small bowel kinking by the growing uterus. Sigmoid volvulus can be treated with colonoscopy. The success rate is lower in advanced pregnancy when a large uterus does not allow

detorsion of the colon. Other causes necessitate early surgical intervention to save both the mother and the fetus.

## 18.1 General Considerations

*Women in a state of pregnancy may be purged, if there be any urgent necessity (or, if the humors be in a state of orgasm?), from the fourth to the seventh month, but less so in the latter case. In the first and last periods, it must be avoided.*

(Hippocrates)

*Let an abdominal scar on a pregnant woman be a line of evidence denoting potential obstruction.*

(Stafford Mathews and PR Mitchell, 1948 [1])

Intestinal obstruction in pregnancy is a consequence of various etiological factors, as in the nonpregnant population. According to the cause of obstruction, various therapeutic options are available. Therefore, depending on the cause, type, duration, and surgical intervention, the maternal and fetal prognosis is also variable.

### 18.1.1 Historical Perspective

Houston published the first case of bowel obstruction in pregnancy in 1841 [2]. Fritz Ludwig collected 95 cases in 1913 [3]. Ley-Klotz et al. found the tight band on the left flank of the gravid uterus causing mechanical obstruction with the cecum extremely distended and the rectum and sigmoid colon empty. A cecostomy was done, with recovery [4]. The first English language series was by Eliason and Erb in 1937 [5]. Two other extensive reviews included reports of 150 cases by Goldthorp in 1966 [6] and 64 cases by Perdue et al. published in the English literature from 1966 to 1991 [7].

### 18.1.2 Incidence

Incidence varies from 1/1500 to 1/66,431 [7]. Before 1940, when surgery was not so common, the reported incidence was 1/1500–1/66,431 deliveries [8, 9]. In the next several decades, with the more widespread use of surgery and decreasing postoperative mortality, the incidence increased from 1/12,000 deliveries to 1/3161 deliveries (Table 18.1). This large range is due to several reasons: (1) general failure to report this complication in the literature, (2) some cases are published in journals not indexed in common medical databases, and (3) over a century of publishing, surgical instruments, and techniques evolved significantly but with a different use in developed and undeveloped countries.

Common causes of intestinal obstruction in pregnant include adhesions (mostly postopera-

tive), volvulus, and intussusceptions [7, 10, 11]. Intra-abdominal adhesions cause 60–77% of intestinal obstructions in pregnancy [7, 10, 11]. Isolated small bowel obstruction (SBO) has an incidence of 1/17,000 pregnancies [12]. Mathews and Mitchell’s statement *let an abdominal scar on a pregnant woman be a line of evidence denoting potential obstruction* should always be remembered by obstetricians and surgeons alike. Intestinal volvulus is responsible for 25% of bowel obstructions in pregnant women but only 3–5% in nonpregnant patients [7, 10, 11]. Although incarcerated groin hernias are the second most common cause of intestinal obstruction in the general population, these cases account for less than 5% of obstructions during pregnancy [13] and intestinal intussusception [14–16].

The increasing incidence of bowel obstruction during the last century is due to the following:

- Older primiparas/multiparas,
- Higher incidence of prepregnancy abdominal operations,
- Decreased postoperative mortality,
- World population growth.

Probably, the slowdown of an increase in the incidence of adhesive obstruction will result from the more widespread use of laparoscopy. Laparoscopy reduces adhesion formation by 100% in the upper abdomen compared to laparotomy [17]. In the lower abdomen, the symptomatic adhesion formation was similar [18]. This should be differentiated from symptoms caused by adhesions—this is the only incidence of adhesion formation. There has been considerable controversy regarding the pregnancy period when an obstruction is most likely to occur. Both Ludwig [3] in 1913 and Johann von Mikulicz-Radecki in 1926 [19] suggested the periods of increased incidence:

4–5th month when the uterus ascends from the pelvis,

**Table 18.1** Incidence of intestinal obstruction during pregnancy in Queen Charlotte’s Hospital and District, 1930–1964

| Year    | Rate     |
|---------|----------|
| 1930–34 | 1/19,940 |
| 1935–39 | 1/8919   |
| 1940–44 | 1/12,214 |
| 1945–49 | 1/18,445 |
| 1950–54 | 1/3494   |
| 1955–59 | 1/2888   |
| 1960–64 | 1/3161   |

Reproduced with permission from [23]

8–9th month when the fetal head descends into the pelvis,  
Delivery and early puerperium when rapid involution uterine size occurs.

Some claim that most cases of intestinal obstruction in pregnancy present during the 3rd trimester [20–22], and obstruction most commonly appears during the first pregnancy after surgery. Large bowel obstruction is less common than SBO [7].

18.1.3 Clinical Presentation

The problem with intestinal obstruction is a large scale of severity of obstructive symptoms and signs, which depend upon:

- Location of the obstruction,
- The degree of obstruction,
- The rate of progression of obstruction,
- Intestinal perforation,
- Underlying malignancy.

The average duration from the onset of symptoms to hospital admission ranges from 48 to 84 h. Once admitted, an average of 48–60 h passes before definitive surgery. An average delay of 4 days remains a significant factor in high morbidity and mortality in the pregnant population.

All colicky pain in pregnancy is not necessarily uterine, and premature labor can complicate intestinal obstruction and vice versa [24].

18.1.4 Differential Diagnosis

The most common conservatively treated differential diagnoses are discussed. The most common differential diagnoses are presented in the sections with specific causes of obstruction.

18.1.4.1 Constipation

Constipation is one of the most common medical conditions affecting the general population. Constipation is second only to nausea, the most common gastrointestinal complaint in pregnancy. Patients with no history of bowel symptoms may develop constipation for the first time during pregnancy. The symptoms often worsen with pre-pregnancy constipation. The prevalence of functional constipation, defined by the *Rome IV criteria* (Table 18.2), is 35%, 38–39%, 20–21%, and 17% in the first, second, and third trimesters, and the postpartum period, respectively [25, 26]. Others found that slightly fewer primiparous women (35%) had constipation during pregnancy compared to multiparous women (39–42%) [27]. Symptoms of incomplete evacuation were the highest in the first trimester (21% decreasing to 12.5% in the puerperium) [28]. Overall, the sensation of incomplete evacuation and the time spent defecating were higher in all three trimesters of pregnancy than in the puerperium. Sensations of urgency decreased as pregnancy proceeded and leveled off in the third trimester. The urgency increased by 24% postpartum compared with levels during gestation. There were no differences between lactating and nonlactating mothers. The causes of constipation in pregnancy are likely multifactorial, including dietary fac-

**Table 18.2** *Rome IV criteria* for the diagnosis of irritable bowel syndrome (criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis)

|                                                                                                                       |
|-----------------------------------------------------------------------------------------------------------------------|
| 1. Must include two or more of the following:                                                                         |
| Straining during at least 25% of defecations                                                                          |
| Lumpy or hard stools in at least 25% of defecations                                                                   |
| The sensation of incomplete evacuation for at least 25% of defecations                                                |
| The sensation of anorectal obstruction/blockage for at least 25% of defecations                                       |
| Manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation and support of the pelvic floor) |
| <3 defecations per week                                                                                               |
| 2. Loose stools are rarely present without the use of laxatives                                                       |
| 3. Insufficient criteria for irritable bowel syndrome                                                                 |

tors, lifestyle issues, and hormonal and mechanical changes. Investigations are aimed at excluding treatable disorders such as hypothyroidism or hypercalcemia. A full blood count, thyroid-stimulating hormone (TSH), serum calcium, and glucose should be performed in all patients presenting with constipation.

The *Rome IV criteria* are a standard clinical measure of assessing chronic constipation but were not formulated with pregnancy-related constipation in mind (Table 18.2). Patients report symptoms relating to the frequency and difficulty in the passage of stool that may not conform to strict diagnostic criteria. Patients may focus on symptoms such as straining, hard stools, unproductive urges, and a feeling of incomplete evacuation. It is, therefore, possible that a patient may report constipation even when they have regular daily stools. A simplified set of criteria for the diagnosis of constipation includes the low frequency of stools (<3 per week), hard stools, and defecation difficulties. These criteria are easier to use in routine clinical practice and are a good indicator of constipation in pregnant women.

As with any medication in pregnancy, laxatives should be used with caution (Table 18.3). Anthraquinone laxatives such as dantron are associated with congenital malformations [29]. Saline osmotic laxatives (magnesium citrate and sodium phosphate) can cause maternal sodium retention, while castor oil can initiate premature uterine contractions. Some laxatives can even produce neonatal diarrhea. Stimulant laxatives such as Senna should be used cautiously in pregnancy because Senna can be excreted in breast milk [30]. In general, the short-term use of stimu-

lant laxatives is considered safe in pregnancy. However, as with the general population, long-term use should be avoided.

*The American Gastroenterology Association Position Statement* considers polyethylene glycol (PEG) to be a low risk in pregnancy and the preferred treatment for chronic constipation in pregnant women [31].

PEG acts as an osmotic laxative by opposing the dehydration of bowel contents that would ordinarily lead to increased stool bulk. The increased retention of water in the colon lubricates and softens the stools. The small amounts (1–4%) absorbed are excreted unchanged in the urine. Lactulose, glycerin, and sorbitol are generally considered safe [31].

Fiber-containing bulking agents such as Metamucil, Citrucel, and Perdiem are probably the safest laxatives to be used in pregnancy, as they are not systemically absorbed [31].

These agents take several days to exert their effects and are unsuitable for acute symptom relief. They are also contraindicated in fecal impaction. They can be used over long periods in patients with uncomplicated constipation. Adverse events related to bulking agents include excessive gas, cramps, and abdominal bloating.

**Table 18.3** Laxatives in pregnancy

| Safe                      | Caution                  | Unsafe                   |
|---------------------------|--------------------------|--------------------------|
| Lactulose                 | Saline osmotic laxatives | Anthraquinones (dantron) |
| Glycerin                  | Castor oil               | Tegaserod                |
| Polyethylene glycol (PEG) | Senna                    |                          |
| Bulking agents            | Docusate sodium          |                          |

**18.1.4.2 Irritable Bowel Syndrome**

Irritable bowel syndrome (IBS) is a functional bowel disorder in the absence of any known abnormality of structure, affecting 9–12% of the general population. The *Rome IV criteria* define



IBS as the presence of abdominal pain associated with a change in the frequency or form of stool (Table 18.2). These symptoms must be present on at least three occasions per month over 3 months. When the patient has hard or difficult-to-pass stools greater than 25% of the time, with loose or watery stools less than 25% of the time, the diagnosis is constipation-predominant IBS (IBS-C). IBS is more common in females and is most frequently diagnosed between 30 and 45 years (i.e., the main reproductive years). It is, therefore, easy to see how constipation-predominant IBS can overlap with gestational constipation.

Tegaserod (5HT<sub>4</sub> agonist) has shown considerable promise as a treatment for constipation-predominant IBS. AGA initially considered tegaserod to be low risk in pregnancy [31]. However, an increased incidence of ischemic cardiac resulted in the Food and Drug Administration (FDA) suspension of tegaserod. Safe drugs used for idiopathic constipation can be used in constipation-predominant IBS.

#### 18.1.4.3 Postpartum Acute Intestinal Pseudo-Obstruction

##### Incidence and Risk Factors

Ogilvie's syndrome (OS), described in 1948 by Sir William Heneage Ogilvie [32], is an acute colonic pseudo-obstruction without a mechanical cause. OS in pregnancy is extremely rare, but 10% of cases reported are related to obstetric and gynecological procedures. One report suggests the incidence of the postpartum OS to be 1:1460 deliveries [33]. In 1976, of all published cases, 35% were after the cesarean section (CS) or vaginal delivery [34]. Most colonic perforations from OS develop during the first several days following CS [35, 36], with two reports in the English literature after "normal" vaginal delivery [37, 38]. The risk factor is opiate use, which is common after CS [33]. Risk factors in the general population such as trauma, severe burns, abdominal or pelvic surgery, sepsis, electrolyte imbalance, spinal trauma/surgery, renal trauma/surgery/transplant, malignancy, congestive cardiac failure, and hip

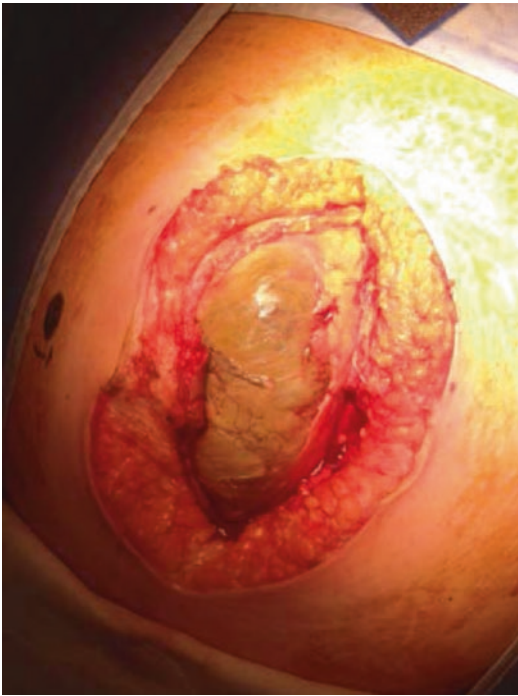
replacement and bed rest possibly increase the risk of OS in pregnancy [39].

##### Pathophysiology

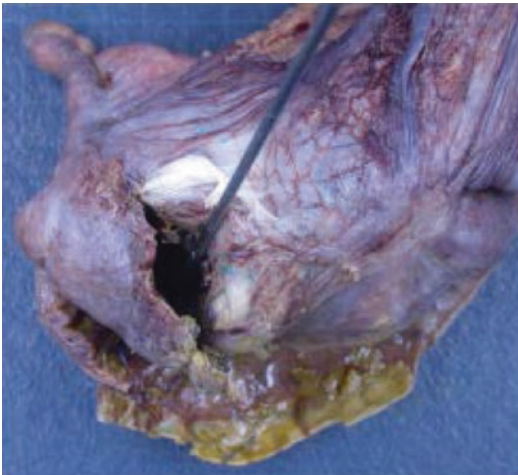
Pathophysiology of OS is [40] reflex motor inhibition through splanchnic afferents in response to noxious stimuli, excess sympathetic motor input to the gut (intestine does not contract), excess parasympathetic motor input to the gut (intestine does not relax), decreased parasympathetic motor input to the gut (intestine does not contract), excess stimulation of peripheral micro-opioid receptors by endogenous or exogenous opioids, and inhibition of nitric oxide release from inhibitory motoneurons. The mechanism of the condition involves loss of tone in the parasympathetic nerves S2–S4. This results in an atonic distal colon and pseudo-obstruction due to the location of autonomic nerves close to structures at risk during CS, including the cervix and the vagina.

Various sources report a cutoff sign relating to an area of dilated and collapsed bowel around the splenic flexure corresponding to the transition zone between the vagal and sacral parasympathetic nerve supplies [39]. The cutoff sign is used to support the hypothesis of parasympathetic inhibition causing OS [39]. However, the actual pathogenesis is likely multifactorial. The association between OS and vaginal delivery may be due to the declining serum estrogen levels in the postpartum period [41]. In the case of OS following normal vaginal delivery, the histological findings of the cecal perforation show no specific pathology [37].

Progression of cecal distension leads to cecal necrosis (Fig. 18.1) or serosal tears with massive distension. These conditions can coexist. With delayed surgery, the final event is cecal perforation [33, 35, 42] with localized or diffuse peritonitis. According to Laplace's law, perforation occurs mostly in the right colon and cecum. Cecal perforation is more common on the anterior tenia (Fig. 18.2) due to ischemia secondary to increased intraluminal pressure. It prevents filling the terminal anterior and posterior cecal arteries, which anastomose on the antimesenteric surface.



**Fig. 18.1** A thin-walled gangrenous cecum 2 days after Cesarean section. (Reproduced with permission from [33])



**Fig. 18.2** Cecum with 4 × 4 cm perforation (no evidence of acute appendicitis or colitis) with surrounding exudate. (Reproduced with permission from [38] under the CC BY 2.0)

### Clinical Presentation

The diagnosis of OS in pregnancy and puerperium is considered troublesome due to nonspecific clinical features [37]. The common clinical

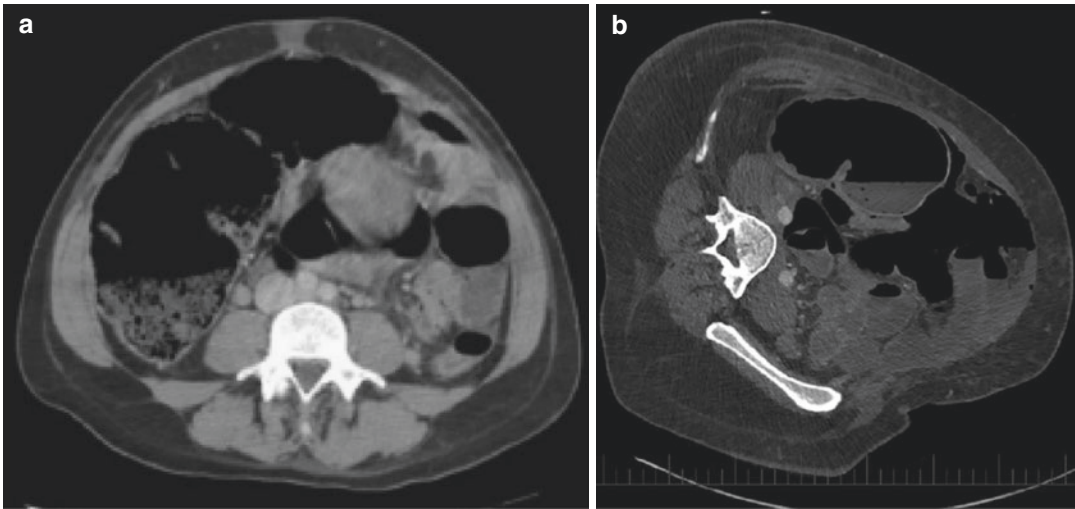
feature is significant abdominal distention [39]. Progressive abdominal distension is often painless at first. Importantly, bowel sounds are usually present and may be normal. Although patients may continue to pass small amounts of flatus or stool, the colonic function is generally inadequate. Abdominal pain, tenderness, and low-grade fevers are common, while nausea and vomiting are rare [40]. Diagnosis should be considered after CS when normal postoperative ileus is common but not prolonged and exaggerated as in OS [43].

### Diagnosis

Serum electrolyte levels are essential with intestinal obstruction, and 83% demonstrated at least one electrolyte disturbance, with hypocalcemia being the most common [39]. Plain abdominal radiographs are generally diagnostic with significant colonic distention (cecal diameter  $\geq 7$  cm), with minimal or no distention of the small intestine [40]. Abdominal radiography is a standard first-line investigation, and a cecal diameter  $\geq 9$  cm (Fig. 18.3) is a sign of imminent perforation [37]. Serial plain abdominal X-rays detect the progression of colonic distension [33] or perforation with a large volume of free gas under one or both hemidiaphragms with multiple abnormally dilated loops. In these situations,



**Fig. 18.3** Plain supine abdominal radiograph shows colonic dilation with no free air. (Reproduced with permission from [35] under the CC BY 3.0)



**Fig. 18.4** Abdominal CT shows (a) colonic dilation with a cecal diameter of 8 cm. (Reproduced with permission from [35] under the CC BY 3.0) and (b) free intraperito-

neal gas and fluid indicating bowel perforation. (Reproduced with permission from [33])



**Fig. 18.5** Berthold Ernest Hadra (1842–1903), physician and surgeon, was born near Breslau, Prussia (now Wrocław, Poland). He obtained his medical education from the universities of Breslau and Berlin. He was appointed the chairman of Surgery at Texas Medical College at Galveston in 1888 and helped transform that institution into the University of Texas Medical Branch at Galveston. He received international respect for his pioneer work in the fields of surgery and gynecology. (Courtesy of *American Association of Neurological Surgeons*, 2004) [55]

serial serum WBC, neutrophils, and CRP rise significantly. CT is used in doubtful cases to define (1) other etiologies of obstruction, (2) the diameter of the cecum (Fig. 18.4), (3) bowel wall gas as a sign of bowel ischemia, and (4) free gas and fluid as a sign of perforation of a distended bowel (Fig. 18.5).

### Conservative Treatment

Initial management should include IV fluid therapy and nasogastric suction. Patients should be fasting; if possible, all narcotic analgesics should be stopped. Colonoscopic decompression is highly successful unless signs of peritonism are evident, although recurrence is common [39]. Pharmacological treatment includes naloxone, cholinergic stimulation with neostigmine or erythromycin, and cisapride, although the benefit in idiopathic OS is uncertain. Some support the use of laxatives in the postpartum period [41]. The most important potential complication of conservative treatment is large bowel perforation with subsequent fecal peritonitis.

### Surgical Treatment

In the general population, surgical treatment is indicated when:

- Cecal diameter >9 cm,
- Progression of cecal distention or failure of resolution after several days,
- Evidence of perforation,
- Unsuccessful colonoscopy,
- Recurrence after successful colonoscopy.

Even guidelines from 2020 of the *American Society for Gastrointestinal Endoscopy* do not mention the pregnant population [44]. Surgical management depends on intraoperative findings. If cecal distension without necrosis is found, cecostomy with appendectomy is indicated. Ischemic or gangrenous bowel mandate limited or formal right hemicolectomy with primary anastomosis. Hemicolectomy with a double-barrel stoma is preferred with cecal perforation (Fig. 18.4b) and stercoral peritonitis.

### Prognosis

As almost all cases develop after delivery, the fetal outcome is excellent. The maternal outcome is excellent because most cases are cured with conservative therapy [33]. In surgically treated patients, maternal mortality is almost nil, but morbidity depends on the delay of abdominal exploration and progression and extension of stercoral peritonitis from a bowel perforation.

### 18.1.5 Treatment

Conservative and surgical therapy for intestinal obstruction during pregnancy is discussed for every disease separately. For total parenteral nutrition, see Sect 2.3.2.

### 18.1.6 Prognosis

#### 18.1.6.1 Maternal Outcome

In 1900, maternal mortality from intestinal obstruction reached 60% [45], and in 1937, it was lowered to 21% [7]. A further decline in maternal mortality was in 1966, with a reported incidence of 12% [6, 23]. In recent series, maternal mortality decreased to 6%. Maternal mortality by etiology is presented in this chapter.

#### 18.1.6.2 Fetal Outcome

Intestinal obstruction in the second trimester caused premature labor with subsequent neonatal death in 33% [46], whereas the perinatal loss in the third-trimester obstruction was 47% [47].

Neonatal mortality remains high, 20–26%, while around 1937 was 50% [7]. Hypoxia and hypotension during anesthesia should be prevented as these are significant factors for fetal death.

## 18.2 Intussusception

### 18.2.1 General Considerations

Intussusception was usually fatal until the early twentieth century. John Hunter described the clinicopathological characteristics. Sir Fredrick Treves, an eminent nineteenth-century surgeon, described the treatment plan, which by and large remains valid to date [48]. Adult intussusception is rare and present in 1/30,000 of all hospital admissions, 1/1,300 of all abdominal operations, 1/30–1/100 of all cases operated for intestinal obstruction, and one case of adult intussusception for every 20 childhood ones [49]. The mean age at presentation tends to be in the sixth decade of life [49, 50]. Higher age at intussusception may point to underlying malignancy since the mean age for benign cases is 44 years as opposed to 60 years for malignant [50]. Approximately 80–90% of adult intussusceptions are secondary, typically associated with tumors, granulomas, foreign bodies, or an anatomic defect. Adult small bowel intussusceptions are secondary to benign lesions in most cases, with malignant lesions causing 15% of cases and idiopathic intussusceptions accounting for approximately 10–20% [51]. The male-to-female ratio is 1:1–1.3 [52]. This entity can be classified into four distinct categories [50]:

- *Enteric*, in which the intussusception is confined to the small bowel,
- *Ileocolic*, in which the ileum invaginates through a fixed ileocecal valve,
- *Ileocecal*, in which the ileocecal valve itself is the lead point for the intussusception,
- *Colocolic*, in which the lead point is restricted to the colon.



It may be acute or chronic (persistent or intermittent) in addition to being “silent” [53]. The chronic intussusception may have lasted, in some instances, for a year before the diagnosis. Although surgical intervention is necessary for small bowel intussusception in symptomatic adults, many asymptomatic and likely transient intussusceptions may be incidentally detected on CT.

## 18.2.2 Historical Perspective

The first known cases of intussusception in pregnancy are the intussusception of the rectum described by Berthold Ernest Hadra (Fig. 18.5) in the *Richmond and Louisville Medical Journal* in 1876 and by Williamson in 1914 as the jejunal intussusception through gastroenterostomy after vaginal delivery of stillbirth in the 34th week of her second pregnancy. Before her first pregnancy, she was operated on twice due to a peptic ulcer [54].

## 18.2.3 Incidence

### 18.2.3.1 Pregnancy

The incidence of intussusception is similar in pregnant and nonpregnant women [56]. Intussusception as a cause of intestinal obstruction was found in 5–6% [7, 57] of pregnant patients with intestinal obstruction. The most common location of intussusception was ileocecal [56, 58, 59]. Meckel’s diverticulum is the most common precipitating factor in pregnancy [60]. Chaffen, Mason, and Slemons, in 1937, collected 20 cases associated with pregnancy and puerperium [61]. In one study, 30% (3/10) of intestinal obstructions during pregnancy were from intussusception [22]. There are only several cases of primary intussusception in pregnancy published. Probably this is due to the bimodal incidence of intussusception—in childhood and with increasing incidence during life, with the second peak in the sixth decade of life. Williamson published one of the first postoperative invaginations (see Sect. 18.2.2). Increased use of bariatric

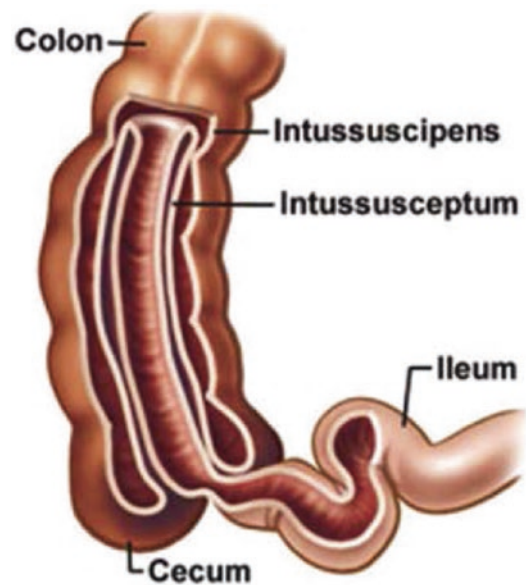
surgery results in an increased rate of intussusception during pregnancy (see Sect. 23.2) and internal hernia incarceration (see Sect. 23.3).

### 18.2.3.2 Puerperium

An idiopathic intussusception after normal vaginal delivery is possible [62]. Two cases of post-CS intussusception have been published. One case is secondary to colonic adenocarcinoma, and another to idiopathic ileoileal invagination 80 cm proximal to the ileocecal valve in women with preeclampsia, which was manually reduced [63].

## 18.2.4 Etiopathogenesis

Masses in the bowel or lumen act as an irritant and provoke abnormal peristaltic movement, leading to the telescoping of one bowel segment over the adjacent segment. Intussusception is a complex soft tissue mass consisting of the outer intussusciens and the central intussusceptum (Fig. 18.6). A tumor acting as the lead point of



**Fig. 18.6** Schematic drawings of intussusception. The longitudinal section of intussusception shows the invagination of one segment of the gastrointestinal tract (intussusceptum) into the adjacent segment (intussusciens). (Reproduced with permission from [64])



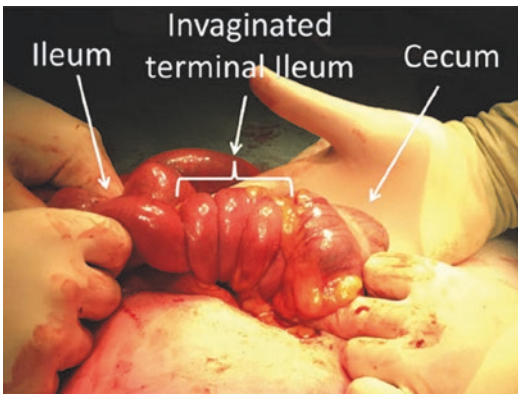
intussusception may be outlined distal to the tapered lumen of the intussusceptum. The cause of intussusceptions in adults varies by location. Large bowel lead points are more frequently malignant than small bowel lead points.

#### 18.2.4.1 Pregnancy

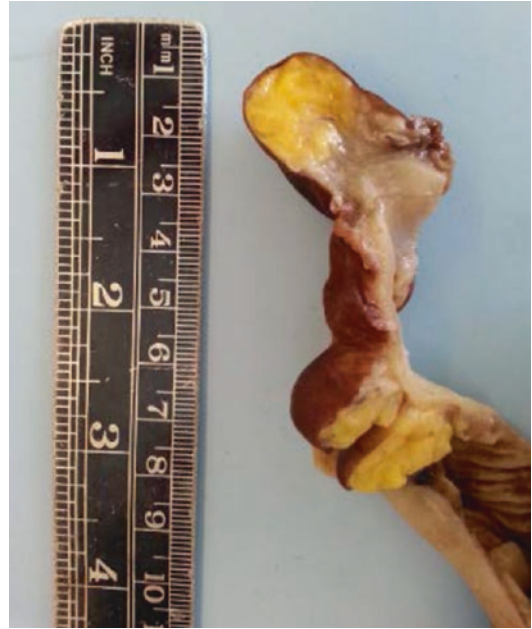
It is unclear how pregnancy contributes to the development of intussusception or whether it is just a coincidence. Most patients without the lead point are in the second or third trimester [20, 65–68]. The long-standing obstipation, common in pregnancy, and the direct pressure of the gravid uterus on the rectum, could result in intussusception without the leading point.

#### 18.2.4.2 Intraluminal Pathology

Various pathologic conditions, as leading points, can be present and found as early as the 8th week of pregnancy [58]. These include hamartomatous polyp [60], lipoma [58], benign neurilemmoma [69], and primary non-Hodgkin's lymphoma [70, 71]. Meckel's diverticulum is the most common [72]. Even the heterotopic pancreas causes intussusception during pregnancy [15]. It is postulated that there is a relationship between the enlargements of a heterotopic pancreas with the hormonal changes in gestation [73]. In pregnancy, the most common is ileocecal intussusception (Figs. 18.7 and 18.8). Colonic leading point in pregnancy has a higher incidence of malignancy [74].



**Fig. 18.7** The ileocecal intussusception in 8 weeks of pregnancy. The terminal ileum was “telescoped” into the lumen of the caecum and the ascending colon. (Reproduced with permission from [58])



**Fig. 18.8** Macroscopic cross sections showed several lipomatous tumors in the terminal ileum located under the mucosa. (Reproduced with permission from [58])

#### 18.2.4.3 Bariatric Surgery

See Sect. 23.2.

### 18.2.5 Clinical Presentation

The clinical presentation of adult intussusception varies considerably. Presentation depends on the following:

- Location of intussusception,
- The rapidity of obstruction,
- Duration of intussusception,
- Underlying cause.

The most common symptoms of intussusception are abdominal pain, nausea, and vomiting; less frequent symptoms are melena, weight loss, and fever and could be of long duration (several weeks to several months) if the intussusception is intermittent or partial, although the patient may

occasionally present with complete mechanical obstruction with bowel gangrene [51]. Common physical findings include abdominal distention, decreased or absent bowel sounds, and abdominal mass [50, 59]. A diagnosis of adult intussusception is equally challenging because the classical pediatric triad of intussusception (acute abdominal pain, palpable “sausage-shaped” mass, and “red currant jelly” stools) is seldom observed.

In a pregnant woman after Roux-en-Y gastric bypass, the duration of symptoms varied from hours to weeks [75]. A common sign is tenderness on palpation in the left upper quadrant.

In advanced pregnancy, it may not be possible to palpate a mass [20]. Palpable mass can be found up to 22 weeks gestation [16, 59]. A malignant cause of intussusception is more likely to present with a shorter duration of symptoms. Sometimes the symptoms can resolve but can recur during the same pregnancy if partial or intermittent intussusception is present [20]. Symptoms of the rectoanal intussusception (internal rectal prolapse) are the sensation of incomplete evacuation, pressure toward the sacrum, which may increase with straining, frequent stools, tiny, slimy, and mixed with blood, and uncontrolled by internal medication, tenesmus, and absence of fever. Diffuse tenderness and guarding are signs of intestinal strangulation, especially if fever is present [76].

Nausea and hyperemesis that occur during normal pregnancy can mask the development of an SBO. The additional diagnostic issue is a presentation during the puerperium. Symptomatology is similar to the pregnant population after normal vaginal delivery [62] or CS [63]. Suspicion should be raised if abdominal pain or distension occurs after a period of normal delivery. Difficulties after CS are encountered because (1) symptoms are attributed to incisional pain and (2) ileus is attributed to early postoperative ileus or acute pseudo-obstruction [77]. Idiopathic postoperative intussusception is more common after abdominal operations and usually occurs within 2 weeks following surgery.

Gynecological examination reveals normal findings with intussusception of any cause [76].

## 18.2.6 Differential Diagnosis

In addition to the standard differential diagnosis of intestinal obstruction, associated medical complications such as acute pancreatitis seen with afferent biliopancreatic limb obstruction after RYGB may draw attention away from the inciting obstruction. The nonspecific nature of abdominal complaints early during RYGB-associated obstruction (see Chap. 23) may incorrectly be attributed to common obstetrical complaints such as morning sickness, hyperemesis, reflux, and uterine contractions.

## 18.2.7 Diagnosis

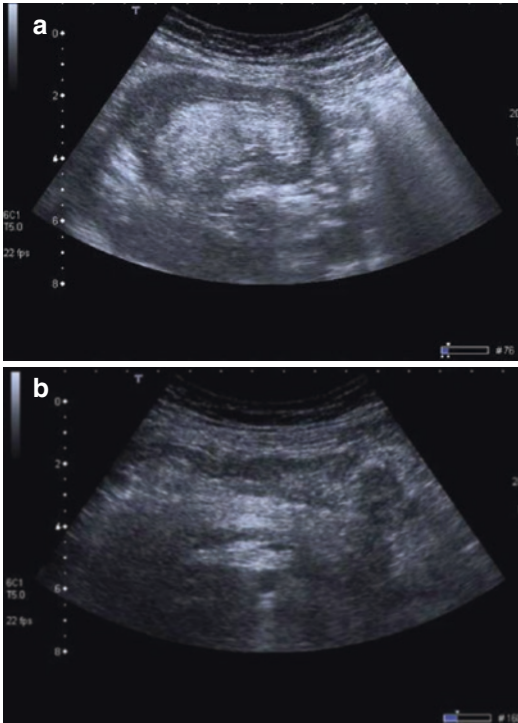
Increased use of ultrasound (US), CT, and improved methods of small bowel examination resulted in accurate preoperative diagnosis of intussusception. In the 11 reported cases of intussusception in pregnancy in the past 25 years, 55% were diagnosed preoperatively. Three cases were diagnosed by the abdominal US, one by plain abdominal X-ray post-delivery, and one by abdominal MRI [57, 60, 65, 78]. In the puerperium, all diagnostic imaging modalities were used [62, 63, 77].

### 18.2.7.1 Plain Abdominal X-Ray

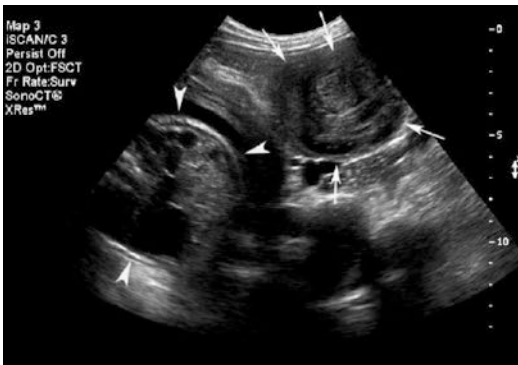
Plain abdominal radiograph findings depend on the degree of intestinal obstruction. With complete obstruction, air–liquid levels are present. Potentially misleadingly normal findings are present with retrograde intussusception after RYGB (see Sect. 23.2).

### 18.2.7.2 Transabdominal Ultrasound

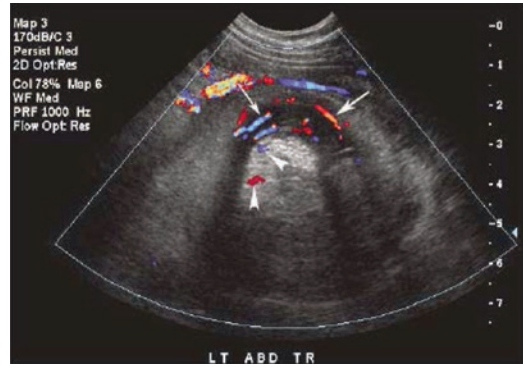
Characteristic sign of intussusception is a “target-like” or “bull’s eye” lesion, similar to the CT findings [78]. The classic features include “target,” “doughnut,” or “crescent-in-doughnut” signs on a transverse view and the “pseudokidney” sign in the longitudinal view (Fig. 18.9), or multiple concentric rings of intussusceptum (Fig. 18.10) or multiple concentric vascular signals in thickened intussusciptens (Fig. 18.11) [16, 60, 62]. The central echogenic area is produced by the mucosa of the intussusception, sur-



**Fig. 18.9** (a) Transverse abdominal sonography: a “bull’s eye” or “doughnut” image with an echogenic center and a translucent rim are visible. (b) Longitudinal ultrasound shows the “pseudokidney” sign, representing the intussusceptum and intussusciens. (Reproduced with permission from [58])



**Fig. 18.10** Jejunojejunal intussusception during late pregnancy. A transverse gray scale sonogram shows multiple concentric rings (*arrows*) representing multiple layers of the innermost intussusceptum, intervening mesenteric fat, and vessels and outer intussusciens on the left side of the fetal abdomen (*arrowheads*). (Reproduced with permission from [60])



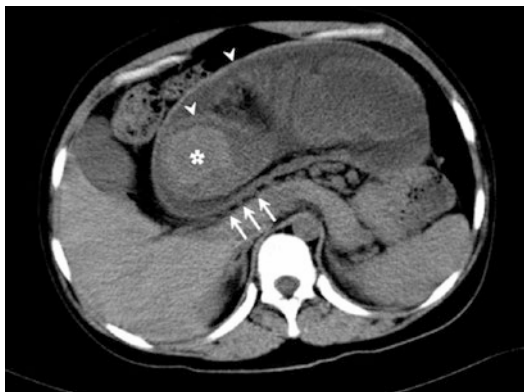
**Fig. 18.11** Jejunojejunal intussusception during late pregnancy. Transverse color Doppler sonogram shows multiple concentric vascular signals in thickened intussusciens (*arrows*) and some vascular spots in the hypoechoic intussusceptum (*arrowheads*) and echogenic mesentery. (Reproduced with permission from [60])

rounded by a hypoechoic ring representing the walls of the intussusceptum and the intussusciens [77]. This variability in appearance is mainly due to the scanning level, the amount of intussuscepted mesentery, the degree of bowel wall edema, and the presence of a pathologic lead point and lymph nodes.

### 18.2.7.3 Abdominal CT

Intussusception on abdominal CT shows a pathognomonic bowel-within-bowel configuration (Fig. 18.12) with or without fat and mesenteric vessels [77]. Intussusception appears as a sausage-shaped mass when the CT beam is parallel to its longitudinal axis but as a target-like mass when the beam is perpendicular to the longitudinal axis [51].

In RYGB patients, abdominal CT is the investigation of choice. Plain abdominal films can be misleading and falsely reassuring due to the high level of obstruction. The significant variability in the different gastric bypass techniques (antegastric or retrogastric Roux loop,



**Fig. 18.12** Plain CT shows a “double circle sign” of the small intestine (*arrowheads*) with a neoplastic lead point (*asterisk*) and mesenteric vascular bands (*arrows*). (Reproduced with permission from [79])

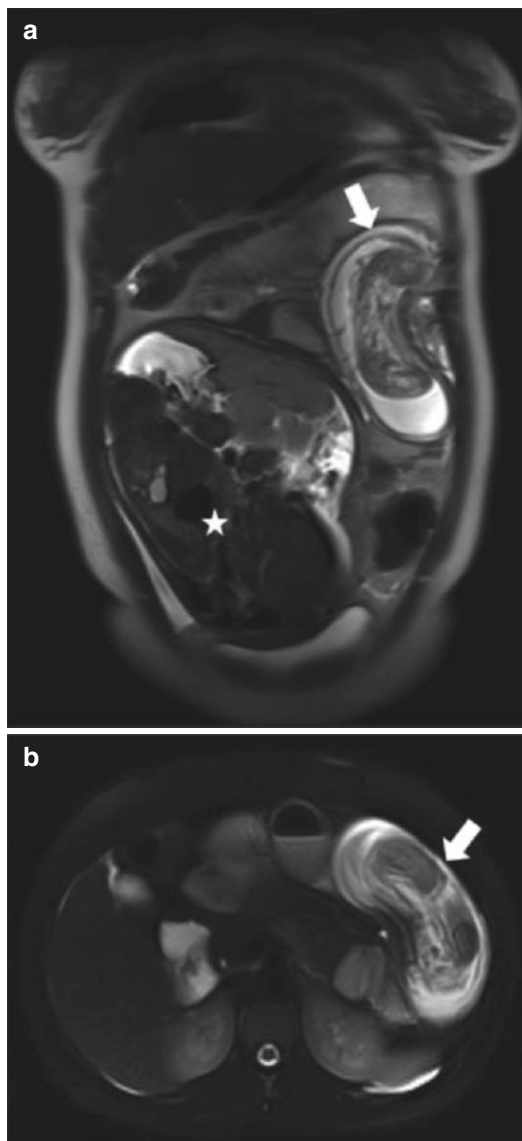
in retrocolic or antecolic configuration) mandates the availability of the patients’ operation notes to facilitate a correct interpretation of the CT findings.

#### 18.2.7.4 Abdominal MRI

MRI is increasingly used (Figs. 18.13 and 18.14). Barium reflux in the lumen between the intussusceptum and intussusciens allows the coiled spring to be visualized. Abdominal MRI was first used to define intussusception during pregnancy in 1992 [57]. In 75%, no leading point was not found [20, 22, 80].

#### 18.2.7.5 Additional Modalities

Rectoanal intussusception (internal rectal prolapse) is made primarily by defecography, which is contraindicated in pregnancy. Anoscopy or rectoscopy reveals the intussuscepted fold and could differentiate it from incarcerated internal hemorrhoids. Dynamic pelvic MRI has the advantage of imaging all compartments of the pelvis and their interaction during defecation. Real-time dynamic transperineal US evaluates all compartments within the pelvis and their interaction at rest, as well as during straining and defecation.



**Fig. 18.13** A MRI of intussusception. T2-weighted HASTE imaging, coronal section (**a**) shows a sausage-shaped intussusception (*arrow*) located superolateral to the gravid uterus (*star*). T2-weighted BLADE imaging, an axial section with fat saturation (**b**) shows the intussusception (*arrow*) located at the left side of the abdomen, anterolaterally to the left kidney. Also, note the increased diameter of the affected intestinal segment with T2 hyperintense changes in the intestinal wall, indicative of edema. A lead point could not be identified. (Reproduced with permission from [80])





**Fig. 18.14** MRI of intussusception in the epigastric region, with the gravid uterus inferior to and separated from the mass. (Reproduced with permission from [65])

## 18.2.8 Treatment

### 18.2.8.1 General Principles

Once the intussusception is suspected, emergency measures should be initiated. Immediate aggressive medical care within the first 24 h is necessary due to the high incidence of necrotic bowel in intussusception. There is an increased chance of death if this disorder is not treated within 48 h. Therapeutic principles for intussusception are the same as in the nonpregnant population:

- Solve the intussusception itself,
- Treat the cause of the intussusception if present.

### 18.2.8.2 Conservative Treatment

The usual measures employed to deal with adhesive bowel obstruction, such as blind nasogastric tube insertion, have no place in RYGB patients as they can lead to bowel perforation at the gastrojejunostomy and a false sense of decompression. At the same time, the biliopancreatic limb can remain obstructed (see Chap. 23).

With colonic intussusception, malignancy and resection are more likely. A therapeutic barium enema can be tried in selected cases with unknown or absent underlying pathology [77]. Rectal intussusception treatment since 1879 consisted of copious injections of cold water with considerable force. These unfolded the invagination and produced natural dejections. In some patients, small bowel intussusception may be an incidental finding. Observation is indicated if imaging does not reveal a lead point, vascular compromise, or bowel obstruction [77].

### 18.2.8.3 Surgical Treatment

Most patients undergo exploratory laparotomy, but recently, laparoscopy has been more frequently used to minimize abdominal wall trauma and shorten hospital stay [63, 77]. This is important to facilitate an earlier return to everyday life and maternal care for the newborn baby.

After exploration, the further procedure depends on the viability of the intestine and the presence of the lead point. The manual reduction can be attempted with viable small bowel intussusception if malignancy is not suspected (palpated or checked with intraoperative enteroscopy) [63]. The manual reduction should be performed by pushing the intussusciptens rather than pulling the bowel due to a lower risk of bowel wall tearing. Resection of the bowel segment is indicated with [62] the following:

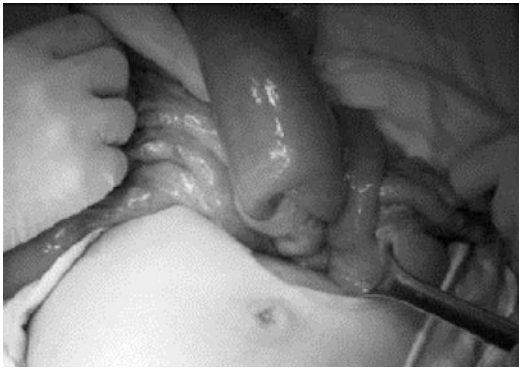
- Gangrenous bowel,
- Recurrent intussusception,
- The leading point.

The leading point should be resected, and further therapy depends on the pathohistological diagnosis (Fig. 18.15).

## 18.2.9 Prognosis

In 1937, mortality was higher in all stages of pregnancy [61]. The prognosis depends on the state of the bowel. Maternal prognosis is excel-





**Fig. 18.15** Jejunojejunal intussusception during late pregnancy. Jejunojejunal intussusception of about 80 cm in length shows a sausage-shaped mass comprising the swollen intussusciptens with an invaginating intussusceptum of more proximal loops. Pedunculated polypoid mass is hamartomatous polyp. (Reproduced with permission from [60])

lent after resection for ischemic bowel or without bowel resection [58, 62, 63, 77, 80]. Higher rates of spontaneous abortion and preterm labor are present [58], mainly if perforation with peritonitis occurs. If intussusception presents during the puerperium, it is easier to indicate diagnostic imaging with radiation; therefore, the diagnosis is made earlier. The problem is that intussusception is sometimes mistaken for postdelivery ileus delaying the diagnostic workup.

## 18.3 Transvaginal Instrumental Uterine Perforation

### 18.3.1 Introduction

Abortion is an extremely sensitive topic. It is unreasonable to expect reliable data about abortion practices in a country such as India, where even vital registration—the recording of births, deaths, and marriages—is incomplete and inaccurate [81]. Most illegal (unsafe) abortions are conducted in the rural areas of developing nations with inadequate facilities, non-sterile instruments, and unqualified personnel, causing an increase in mortality and morbidity [81]. Although rare but important complication is SBO through uterine wall perforation, obstructions of

the large intestine are rarer due to their fixed position. Therefore, large bowel complications are mostly from instrumental perforations. Axel Werelius published one of the first cases of SBO due to evisceration through vaginal introitus in 1907 [82].

### 18.3.2 Incidence

Although rare and uncommon in the developed world, bowel perforation secondary to illegally induced abortion is more common in developing or predominantly undeveloped countries where abortion laws are still restrictive, and most abortions are performed clandestinely and illegally by unqualified personnel [83, 84]. The increased incidence of abortion-related complications, such as bowel injuries, has been reported in most developing countries [85].

First-trimester surgical abortion (as opposed to prostaglandin medical abortion) is one of the most frequently performed procedures in the United States, with a declining incidence—from 1.3 million in 1987 [86] to 853,485 in 2001 [87]. Minor complications (0.846%) are managed as outpatient procedures, including mild infection, resuctioning on the day of the procedure or subsequent resuction, cervical stenosis, cervical tear, underestimation of gestational age, and convulsive seizure after local anesthesia [88]. Major complications (0.071%) requiring hospitalization after the first-trimester surgical abortion include incomplete abortion, sepsis, uterine perforation, vaginal bleeding, inability to complete abortion, and combined (heterotopic) pregnancy [88]. According to WHO, every 8 min, a woman dies due to complications from unsafe abortion, making it one of the leading causes of maternal mortality (13%) [89]. About six million abortions are performed every year in India. Surgical abortion is one of the leading causes of maternal mortality, constituting 20% of maternal deaths [90]. In Pakistan, bowel injuries secondary to unsafe abortion vary from 6 to 22% [91]. The global abortion rate was stable between 2003 and 2008, with 29 and 28 abortions per 1000 women aged 15–44 years, respectively, following a decline

from 35 abortions per 1000 women in 1995. The average annual percent change in the rate was nearly 2.4% between 1995 and 2003 and 0.3% between 2003 and 2008. Worldwide, 49% of abortions were unsafe in 2008, compared to 44% in 1995 [92].

Instrumental uterine perforation is rare, with a reported rate of 0.02–0.17%, while in cases with laparoscopy (tubal ligation at the time of first-trimester abortion), it is visualized in up to 2% [93–96]. The bowel perforation rate as a complication of induced abortion has been reported in 2–18% of all abortion-related complications [97–101]. Bowel injury occurs in 7.5% of uterine perforations [102] and 24% in undeveloped countries with unsafe abortions [103]. Japan has the lowest rate of uterine perforation (0.02%) but the highest rate of intestinal injury (56%) [104]. However, many cases may have been unreported because of their medicolegal implications [105]. In undeveloped countries, unsafe abortion carries a uterine perforation rate of up to 30% [103, 106].

Less than 50 cases of SBO after transvaginal instrumental uterine perforation are published, almost all during the first trimester [91, 107–109]. Second-trimester abortion has a higher rate of uterine perforation than first-trimester abortion [93, 94, 110]. On the contrary, direct bowel injury is more common in the second trimester, with an incidence of 70% [97, 111, 112].

The extremely rare incidence of SBO after uterine perforation due to surgical abortion is due to the following:

- The rare occurrence of instrumental uterine perforation,
- Spontaneous healing of asymptomatic uterine perforations [113],
- Immediate laparotomy/laparoscopy with recognized uterine perforation in 47–84% [95],
- Underreported/undocumented uterine perforation,
- Prehospital mortality, mostly in undeveloped countries [114].

### 18.3.3 Risk Factors

The level of training is the most significant risk factor for uterine perforation [115, 116]. Other risk factors include advanced maternal age, greater parity, retroverted uterus, prior abortion or CS, previous cone biopsy, failure to use US, and underestimation of the duration of pregnancy [93, 94, 117–119]. Uterine perforations are mainly located in the uterine fundus, presumably caused by the introduction of cervical dilators [120] or the posterior wall [91]. Hence, difficulty during cervical dilation also has been associated with a higher perforation rate, and some recommend prostaglandin use to aid in dilation of the cervix [93, 94]. Additionally, prostaglandins contract the uterus, decreasing the perforation rate [95] and minimizing complications such as bleeding or organ prolapse through small uterine perforations.

In Japan, sharp curettage is the most frequently used for a surgical abortion, unlike the Western countries. Apart from risk factors for uterine perforation, the risk factors for SBO after uterine perforation are not completely defined due to a few cases. Several factors could increase the incidence [107, 117, 121, 122]:

- Failed medical abortion,
- Curettage for retained parts of the placenta after a previous pregnancy,
- The diameter of uterine perforation,
- Multiple pregnancies.

Similar risk factors are present for bowel injuries associated with instrumental uterine perforations. Interestingly, some studies have the highest incidence in the second trimester, while others in the first trimester [91]. The location of the uterine perforation predisposes the bowel segment to injury. In anterior uterine perforation, injuries to the small bowel and bladder dominate. In the posteriorly located uterine perforations, injuries to the rectosigmoid part of the large bowel pre-

dominate. In fundal perforations, small and large bowel injuries are found [91, 123]. Along with the uterine location perforation, the segment of the injured intestine is trimester-dependent. During the first trimester, the uterus is placed in the pelvis near the sigmoid colon and rectum, making them more susceptible to injury during the first trimester [98]. With an increase in the size of the uterus, the small bowel becomes more prone to injury during unsafe abortion [124].

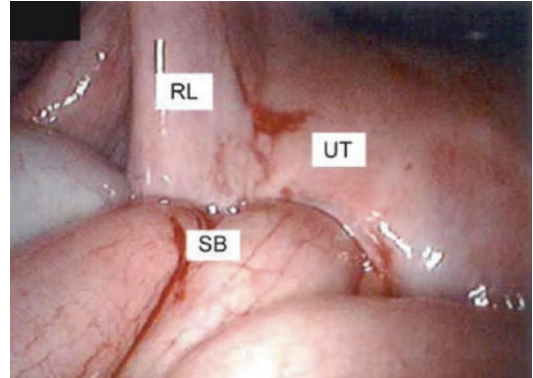
### 18.3.4 Mechanisms of Small Bowel Obstruction

There are four mechanisms of SBO after uterine perforation [107].

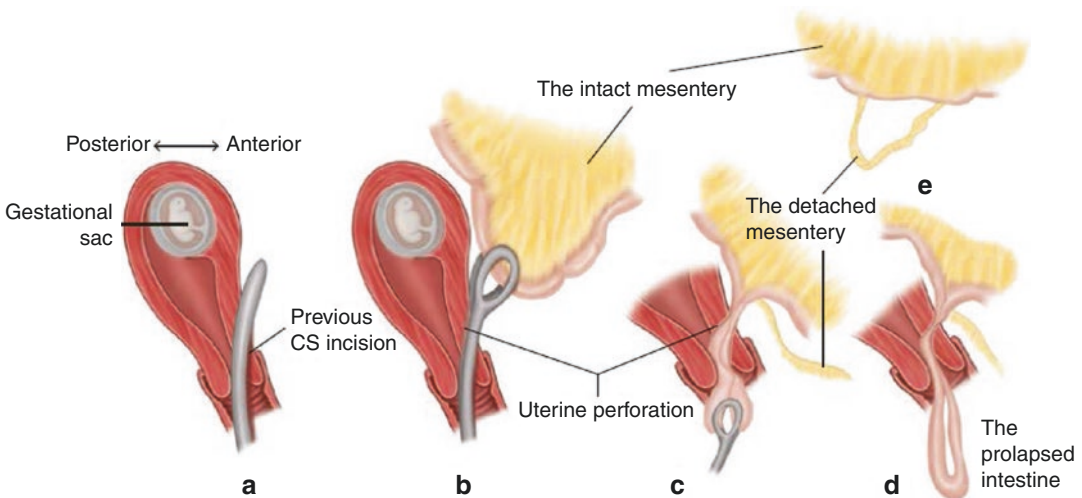
#### 18.3.4.1 Transvaginal Small Bowel Prolapse

Small bowel prolapse (Fig. 18.16) is the most common type. The bowel prolapses through uterine perforation by three mechanisms: (1) *spontaneously* through the larger uterine perforation, enhanced with an increase in intra-abdominal

pressure during pregnancy, (2) by *inadvertent aspiration* [109, 125–129], and (3) the most extensive type results from *inadvertent pulling the small bowel* loops out of vaginal introitus (Fig. 18.17) [114, 115, 122, 130]. Vigorous bowel manipulation is due to pulling the bowel mistaken for the (retained) parts of the fetus or the umbilical cord.



**Fig. 18.16** A defect in the anterior myometrium of the uterus (UT) at the level of the left round ligament (RL), through which the small bowel (SB) has become incarcerated. (Reproduced with permission from [125])



**Fig. 18.17** Schematic of the event. (a) The anterior uterine body wall was perforated with the Hegar dilator. The previous Cesarean section incision was normal. (b) The forceps were extracted from the uterus through the perforation, grasping the ileum. (c) The ileum was pulled through the perforation site. The mesentery was detached when the ileum was pulled through the narrow perforation

site. (d) The ileum prolapsed into the vagina. The ileum was strangulated at the perforation site. (e) The mesentery was completely separated from the bowel, resulting in ileal necrosis. Strangulation at the site of narrow perforation hole (d) may also have caused ileal necrosis. (Modified and reproduced with permission from [131] under the CC Attribution License)

When a small bowel protrudes through the tight opening, an SBO occurs in this increasing order of severity: a simple obstruction, strangulation, mesenteric stripping/detachment, and a small bowel degloving injury. Simple obstruction never occurred through the gravid uterine opening, while 14% developed small bowel gangrene due to strangulation [132].

*Mesenteric stripping*, the third degree of severity of SBO, is a detachment of mesentery from the bare “tube” of the small bowel. This degree is present in 64% [132].

The *degloving injury* is a circumferential tear of the seromuscular layer of the intestine, which separates from the underlying mucosa due to shearing forces and thinned-out mucosa bulging away from the serosa layer along with mesenteric stripping. It is present in 18% [132].

Mesenteric stripping and a small bowel degloving injury result from pulling forces by instruments or examiner’s hands. The progression of SBO does not cause these injuries. Additional confirmations include central degloving injuries and peripheral mesenteric stripping [133] or central mesenteric stripping with peripheral strangulation gangrene [134] as transitional small bowel lesions.

#### 18.3.4.2 Greater Omentum Incarceration

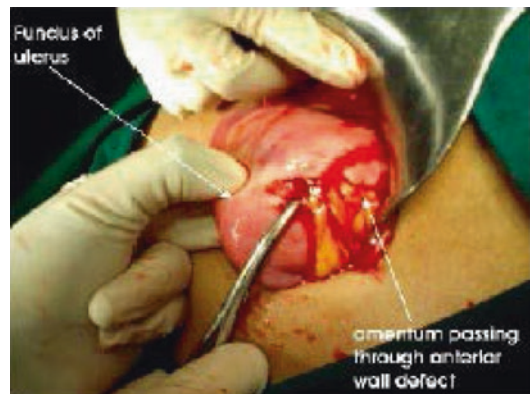
Uterine perforation contains incarcerated herniated greater omentum. A part of a greater omentum can cause compress the small bowel resulting in SBO (Fig. 18.18) [118]. Another mechanism is the small bowel volvulus around the fibrotic or omental bands.

#### 18.3.4.3 Adhesive Small Bowel Obstruction

The third mechanism is when the small bowel is entrapped in adhesions at the site of uterine perforation [136].

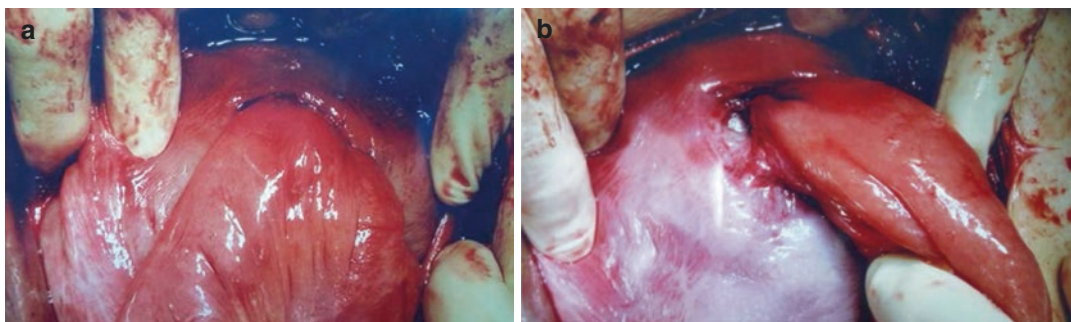
#### 18.3.4.4 Richter’s Hernia-Type of Small Bowel Obstruction

Richter’s hernia-type SBO occurs when the antimesenteric wall of the intestine protrudes through a defect in the uterine wall [128]. The explanation for the symptomless Richter type of SBO follows. During the first pregnancy (2 years previously), a dilation and curettage were performed 4 weeks after delivery to remove the retained placenta. During instrumentation, the uterine wall perforation occurred with Richter type of hernia formation but without the small bowel wall ischemia. In this advanced stage of the second pregnancy, a growing uterus made compression and SBO that was fixed to the uterus previously as a Richter type of hernia (Fig. 18.19). Notably, most (83%) large bowel injuries were associated with posterior uterine wall perforation, whereas 60% of the small bowel injuries were associated with anterior wall or uterine fundus perforation [81].



**Fig. 18.18** Greater omentum incarcerated through the anterior wall defect of the uterus. (Reproduced with permission from [135] under CC Attribution License)





**Fig. 18.19** (a) Richter type of a hernia when the antimesenteric wall of the intestine protrudes through a defect in the uterine wall, causing a partial obstruction that evolves to complete obstruction during a subsequent pregnancy.

(b) The dilated afferent loop is pulled aside to reveal the depth of the uterine perforation. (Reproduced with permission from [121])

### 18.3.5 Clinical Presentation

The uterine perforations are usually recognized during the procedure (dilation and curettage). If the patient signals significant lower abdominal pain, associated injuries should be sought [129]. If unrecognized, most patients have an uncomplicated course with the spontaneous healing of uterine perforations (see Sect. 18.3.2). The type and time of presentation depend on two pathophysiologic processes that could coexist (for instrumental bowel perforation, see Sect. 22.4.2.5):

1. Mechanism of SBO,
2. (Associated) bleeding,
  - (a) From the uterine wall around perforation,
  - (b) From the mesentery detached from its bowel [137].

#### 18.3.5.1 Mechanism of Small Bowel Obstruction

The mechanism of SBO dictates the severity, intensity, and time of presentation of obstruction. The duration of symptoms due to adhesions varies from 4 days to 4 months [107]. These symptoms cause a delay in diagnosis because patients with partial obstruction are commonly managed conservatively [129]. Adhesions can cause partial

or progressive SBO from nonspecific symptoms, including abdominal pain with/without distension to vomiting, (paradoxical) diarrhea, or absence of flatus or stool in later stages. Fever and chills develop in the advanced stage with small bowel gangrene. This should be considered because the intrauterine or intravaginal location of strangulated/detached bowel may mask peritonism [118]. The presentation after 2 years was due to Richter's type of hernia being unpredictable. It can be incarcerated initially at early presentation, or another pathophysiologic event initiates the obstruction. Probably, it partly depends on the size of the uterine perforation [121]. Richter type of incarceration can produce enterouterine fistula (see Sect. 26.6).

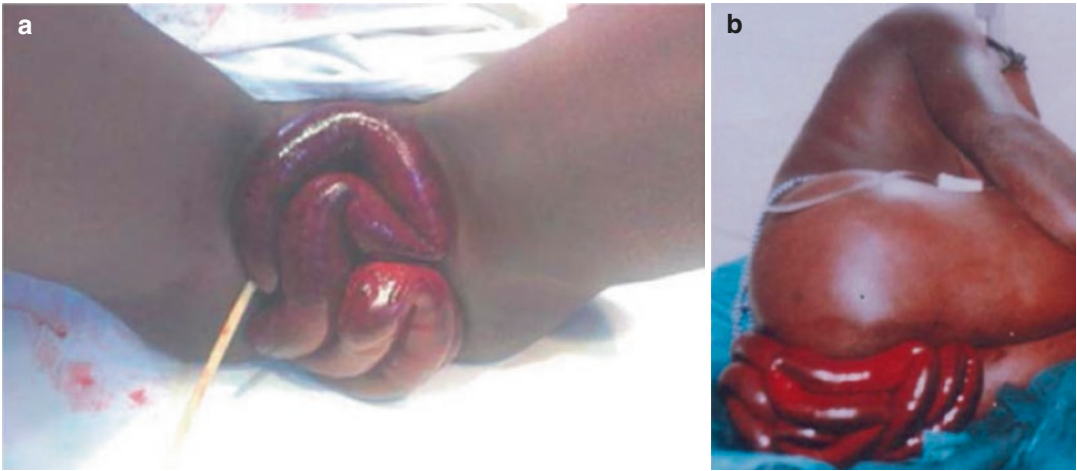
Ischemic bowel perforation is pathophysiologically different from direct bowel injury during instrumental uterine perforation. Such injuries develop a clinical picture within hours after the procedure [138]. If the incarceration of the bowel through the uterine wall is present and not recognized during an abortion and if complete obstruction due to bowel prolapse through the uterine wall is the cause, then the patients present up to several days from uterine instrumentation [107, 123].

Macroscopic small bowel appearance from transvaginal bowel prolapses depends on the



degree of bowel injury and the diagnosis is evident clinically. With strangulation, the vaginal introitus, vulva, and perineum are plugged by protruding, gangrenous loops of the small bowel. The mesentery is not detached, and dilated loops resemble intraperitoneal strangulation. The bowel lumen–mesentery complex is preserved by keeping loops together, making pelvic examination difficult (Fig. 18.20), and the bowel cannot be easily pulled or moved. With mesenteric stripping, the gangrenous small bowel is only a tube with a normal diameter (Fig. 18.21a) or is slightly

thinned out (Fig. 18.21b, c) without attached mesentery (Fig. 18.21d). The degloving injury is an extreme situation, with a circumferential tear of a seromuscular layer of the intestine, separated from the underlying mucosa. The thinned mucosa bulges away from the serosa and mesenteric stripping (Fig. 18.22a). The extremely thinned small bowel is stretched (Fig. 18.22b) without mesentery. With detached mesentery, the small bowel, a tube, can lie down freely outside the body with mesenteric stripping (Fig. 18.21) or degloving injury (Fig. 18.22c).



**Fig. 18.20** (a, b) Small bowel strangulation. With strangulation, the vaginal introitus, vulva, and perineum are plugged by protruding, gangrenous loops of the small bowel. The mesentery is not detached, and dilated loops

resemble intraperitoneal strangulation. The bowel lumen–mesentery complex is preserved, keeping loops together, making further pelvic examination difficult. (Reproduced with permission from [134, 137])



**Fig. 18.21** Mesenteric stripping. The gangrenous small bowel is a tube with (a) a slightly thinned or normal diameter [137] and (b) detached mesentery [131]. With

detached mesentery (c), the small bowel lies freely outside the body [139]. (Reproduced under CC Attribution License)



**Fig. 18.22** Small bowel degloving injury. The degloving is an extreme injury, with (a) circumferential tear of sero-muscular layer, (b) extremely thinned intestine, stretched and without mesentery. (Reproduced with permission

from [140]). (c) As a stretched tube, the small bowels lie freely outside the body, similar to mesenteric stripping. (Reproduced with permission from [141] under the CC Attribution License)

### 18.3.5.2 Small Bowel Obstruction with Bleeding

Any mechanism of SBO could be accompanied by bleeding from either uterine wall perforation or detached mesentery from the bowel. Clinically, bleeding from uterine wall perforation is evident due to transvaginal bleeding, but mesenteric bleeding can present with transvaginal or intra-abdominal bleeding or both. Intra-abdominal bleeding presents as abdominal pain and should always be looked for because the pain can be attributed to abdominal pain caused by coexisting SBO with abdominal distension. It is difficult to conclude whether bleeding or SBO is dominant due to the variations in the severity of obstruction or bleeding. Approximately 39% of patients were hypotensive [107].

## 18.3.6 Diagnosis

### 18.3.6.1 Laboratory Findings

Significant bleeding can be confirmed or excluded with a complete blood count. Blood urea nitrogen and creatinine define hydration. Laboratory findings are needed to correct the metabolic derangements but do not delay an emergent operation, such as vaginal evisceration.

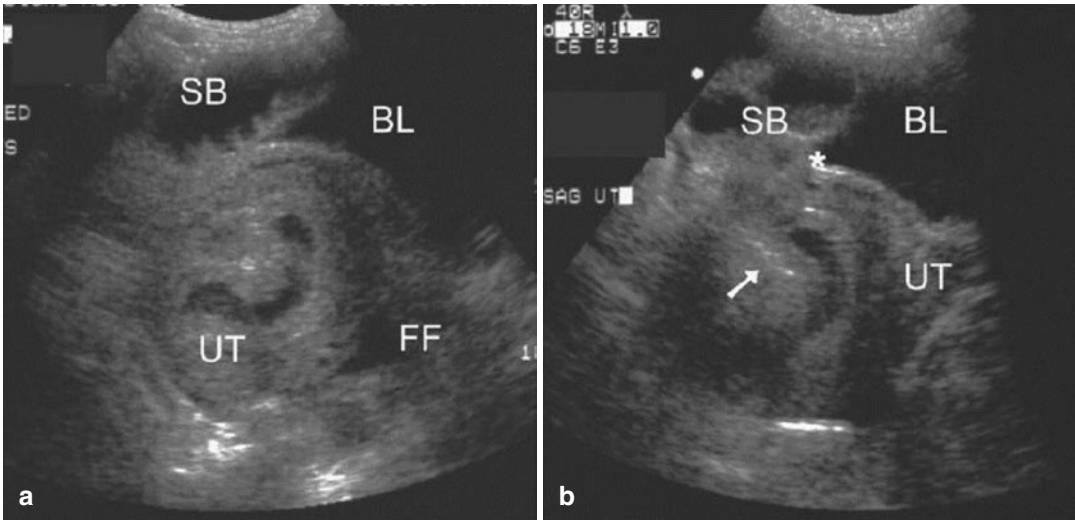
### 18.3.6.2 Plain Abdominal X-Ray

If evisceration is not clinically evident, the diagnosis should be suspected with small bowel air-liquid levels on the plain abdominal X-ray after transvaginal intrauterine instrumentation.

### 18.3.6.3 Abdominal Ultrasound

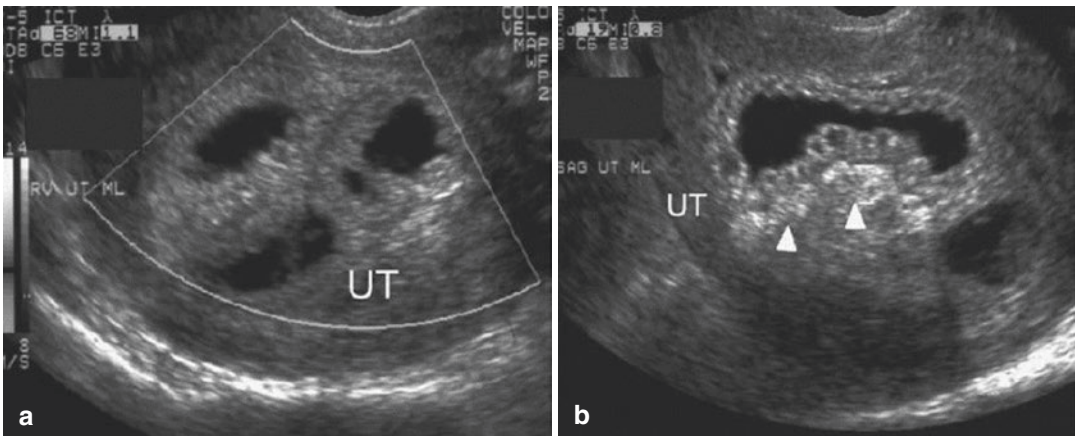
The abdominal US is the preferred diagnostic modality, but the normal appearance of the uterus after a first-trimester surgical abortion can be quite variable. US follow-up after a first-trimester surgical abortion showed that 59% had intrauterine material, initially hyperechoic and later iso- or hypoechoic [142]. No material resembled retained fetal parts or placental parts. The time for the return of the endometrial stripe to baseline appearance was variable, ranging from 1 to 14 days. Similarly, within 1 week of the procedure, only 23% demonstrated reversion to a thin endometrial stripe, 50% displayed a thick endometrial stripe (7–19 mm), and 27% demonstrated an endometrial stripe >20 mm or with very irregular echogenicity >14 mm [143]. There is a trend toward hyperechoic endometrial contents earlier in the week versus hypoechoic contents later in the week, presumably due to liquefying endometrial contents. The appearance of the endometrium after the first menstrual period reverted to normal in all patients. Patient demographics such as gravidity or date of first-trimester abortion did not correlate with the appearance of the uterus.

Dunner et al. made the first report on the US appearance of uterine perforation with suspected bowel entrapment in 1983 [127]. A defect in the uterine wall could be detected with the transabdominal US. The tubular-shaped irregular tissue could be seen within the endometrial cavity, with a small echoic focus suggesting the presence of air (Fig. 18.23). An abnormally increased amount of echogenic free fluid could be seen in the cul-



**Fig. 18.23** (a, b) Transabdominal pelvic ultrasound shows retroverted uterus (UT) adjacent to the urinary bladder (BL) with adjacent fluid-filled small bowel (SB) closely apposed to an interrupted uterine wall (asterisk). A tubular structure is seen within the uterus. A small

amount of anechoic free fluid (FF) is seen in the cul-de-sac. Linear echogenicity (arrow), consistent with the appearance of gas, is adjacent to the abnormal intrauterine tubular structure. (Reproduced with permission from [125])



**Fig. 18.24** (a) Transvaginal pelvic ultrasound transversely shows multiple tubular structures containing anechoic fluid within the uterine cavity (UT); (b) sagit-

tally, echogenic material (arrowheads) suggests the fat adjacent to the intrauterine tubular structure. (Reproduced with permission from [125])

de-sac [125]. The transvaginal US reveals a pelvic free fluid, bowel loops within the myometrial wall, extrauterine fetal parts, or the curette within the myometrium, confirming uterine perforation [144]. The pelvic US could delineate bright, serpiginous, fluid-filled tubular structures within the endometrial cavity (Fig. 18.24). The adjacent material of increased echogenicity could be suggestive of fat. Color Doppler would not show

blood flow in these structures, and no peristalsis would be seen in the intrauterine contents [125].

Apart from defining a uterine perforation, an abdominal US reveals retained intrauterine fetal parts or parts of other intra-abdominal organs [145]. Irregular uterine shadow can wrongly be attributed to incomplete abortion [146]. Free fluid in the Pouch of Douglas or diffusely in the abdominal cavity can be due to bleeding from

uterine perforation or bowel injury with extralumination of its contents, along with potential bleeding from mesentery/mesocolon [146].

#### 18.3.6.4 Abdominal CT

The first reports of CT diagnosis of incarcerated bowel in a uterine perforation were in 2008 by Dignac et al. (incarcerated appendix) and Chang et al. [117, 119]. Abdominal CT is indicated when US is ambiguous or if nongynecologic pathology is suspected. Although the uterine wall can hinder the visualization of intrauterine bowel loops, the bowel's mesentery can be well visualized due to its fatty nature. It should be a red flag for the intrauterine bowel [119]. CT can delineate bowel loops within the uterus (Fig. 18.25).

#### 18.3.6.5 Abdominal MRI

Recently, abdominal MRI has been utilized to assess the endometrial cavity after the first-trimester surgical abortion [147], but this is not routinely performed on an emergent basis. Only one case shows the incarceration of the greater omentum in the uterine perforation without bowel obstruction [148].

### 18.3.7 Treatment

#### 18.3.7.1 Conservative Treatment

Uterine perforations are divided into uncomplicated and complicated. Most uterine perforations recognized during abortion without complications could be managed conservatively [94, 95].



**Fig. 18.25** Pelvic CT after the failure of conservative treatment. Intrauterine mass is an incarcerated small bowel. (Reproduced with permission from [117] under the CC Attribution License)

Many perforations are detected during combined laparoscopy [113]. This implies that the true perforation rate may be underreported and underrecognized without severe consequences to patients, suggesting that conservative management of uncomplicated uterine perforations with close observation is adequate [95, 119, 128].

#### 18.3.7.2 Surgical Treatment

However, the diagnosis or even suspicion of intrauterine bowel/bowel injury (complicated uterine perforation) mandates emergent exploration. Emergent exploration prevents the progression of bowel distention with the development of ischemic necrosis or subsequent bowel perforation. IV fluids and antibiotics (ceftriaxone 2 g and metronidazole 500 mg as starting doses) should be immediately administered.

During exploration, the bowel should be reduced into the peritoneal cavity and evaluated for vitality. The involved herniated bowel may be strangulated, have direct bowel wall trauma, or may be devascularized by coexistent injury or incarceration of the mesentery [129]. In all cases of vaginal evisceration, resection was necessary. In most cases, the minimal resected length was 100 cm, while in 56%, >200 cm was resected. In patients with ileal adhesion, the resection of the ischemic bowel was necessary for 67%. The question is whether the bowel could be saved with earlier diagnosis and treatment. Diversion in the form of a stoma was made in only one patient with complete small bowel resection. It should be performed in patients with hemorrhagic shock or sepsis due to late presentation with gross purulent or fecal contamination of the peritoneal cavity. With isolated SBO without peritonitis, resection with anastomosis is the preferred treatment [107].

When the vaginal wall is the location of small bowel evisceration, the vital bowel can be manually reduced intraperitoneally. Such cases are not possible with uterine perforation because the uterine defect is difficult to close transvaginally. The abdominal US defines a uterine perforation and excludes retained intrauterine fetal parts or parts of other intra-abdominal organs [145] that preclude the transvaginal route of definitive operation.



### 18.3.7.3 Obstetric Management

There are two parts of management. The first deals with uterine perforation/laceration, which should be repaired after treating a small bowel injury. Sometimes uterine perforation should be enlarged to easily pull the bowel into the peritoneal cavity minimizing the possibility of further bowel and mesenteric damage (two patients) [126, 137]. Rarely is a hysterectomy required when the uterus is necrotic or irreparable. The type of bowel injury—obstruction [138, 144] or perforation [146]—does not change the indication for hysterectomy. Hysterectomy was performed in >50% of patients during the first half of the twentieth century and none after 1966 for SBO. For intestinal perforation, a hysterectomy is still performed. Probably, intestinal perforations are associated with more extensive uterine perforations and lacerations [146].

The uterine debridement with suture repair of the uterine defect is the procedure of choice [107].

The perforations <1 cm could be left unsutured, but it is not recommended because there is no long-term follow-up [118].

The second part of the management includes searching intraperitoneally for fetal parts [146]. Most of these abortions are illegal, and there is no medical documentation.

Preoperative consultation with the patient for permanent sterilization should be done because during operation, short additional procedures could prevent repeated complications of further abortions. During exploration, a search for a mutilated fetus should be done [149] with definitive curettage if necessary. Perioperative antibiotics should be administered as indicated for bowel obstruction or bowel perforation. During follow-up, the US of the uterus and  $\beta$ HCG measurement should be performed to eliminate the possibility of retained products of conception [149].

### 18.3.8 Prognosis

Worldwide, there are 30–50 million induced abortions that result in the death of 80,000–110,000 women, of which an estimated 34,000 are in sub-Saharan Africa [116]. Appropriately timed surgical intervention in complicated uterine perforation is crucial to decreasing morbidity and mortality rates. Available data show a survival rate of 93% (two deaths) during the whole century (1907–2012). One patient died due to massive, small bowel necrosis after resection with high jejunostomy. The girl left the hospital against medical advice for social and family reasons and died [81]. The assumption is that high jejunal stoma with high output causes dehydration and electrolyte imbalance, causing death. The second patient had other sigmoid colon laceration treated during the initial operation with resection and anastomosis. The patient became febrile and deteriorated on the fourth postoperative day. The assumption is that colorectal anastomotic dehiscence with diffuse stercoral peritonitis and subsequent septic shock with multiorgan failure developed [122]. An excellent prognosis throughout the whole century is due to the following:

1. The population is young, mostly without comorbidities, and can compensate for significant pathophysiologic stress such as SBO or perforation, sometimes accompanied by various degrees of bleeding. Such conditions could be deleterious for older people, especially those with significant comorbidities.
2. Most patients present with evident SBO either clinically as vaginal evisceration (60%) or during the first 48 h with small bowel in the uterine wall (23%), mostly diagnosed quickly and accurately with the pelvic US. SBO in remaining patients was confirmed with plain abdominal X-ray before perforation ensued.
3. Complications of small bowel resection in young, healthy patients without advanced atherosclerosis are rare, and even long segmental resections have a good long-term prognosis.



## 18.4 Adhesions

### 18.4.1 Definition and Classification

Peritoneal adhesions are pathological bonds usually between the omentum, bowel loops, and the abdominal wall. These bonds may be a thin film of connective tissue, a thick fibrous bridge containing blood vessels and nerve tissue, or direct contact between two organ surfaces [150]. According to their etiology, peritoneal adhesions may be classified as congenital or acquired, which can be postinflammatory or postoperative (the most frequent) [151]. Among postoperative adhesion formation, three processes may be distinguished: *adhesion formation* (adhesions formed at operative sites); *de novo adhesion formation* (adhesions formed at nonoperative sites); and *adhesion reformation* (adhesions formed after the lysis of previous adhesions) [152]. One classification distinguishes two main types of postoperative peritoneal adhesions. Type 1 or *de novo* adhesion formation concerns adhesions formed at sites that did not have previous adhesions, including type 1A (no previous operative procedure at the site of adhesions) and type 1B (previous operative procedures at the site of adhesions). Type 2 involves adhesion reformation, with two separate subtypes: type 2A (no operative procedure at the site of adhesions besides adhesiolysis) and type 2B (other operative procedures at the site of adhesions besides adhesiolysis) [153].

### 18.4.2 Incidence

Intra-abdominal adhesions are associated with 49–77% of SBO in pregnancy [7, 10, 11] due to adhesions from previous abdominal surgery, pelvic surgery, or pelvic inflammatory conditions [7]. Around 50% had a previous appendectomy. Obstruction primarily involves the small bowel, with isolated cases of large bowel obstruction in pregnancy [154]. The terminal ileum is the most

frequent location of adhesive SBO [155–158]. The incidence of intestinal obstruction caused by adhesions during stages of pregnancy is [56] as follows:

- 1st trimester: 6%,
- 2nd trimester: 27%,
- 3rd trimester: 44%,
- Postpartum: 21%.

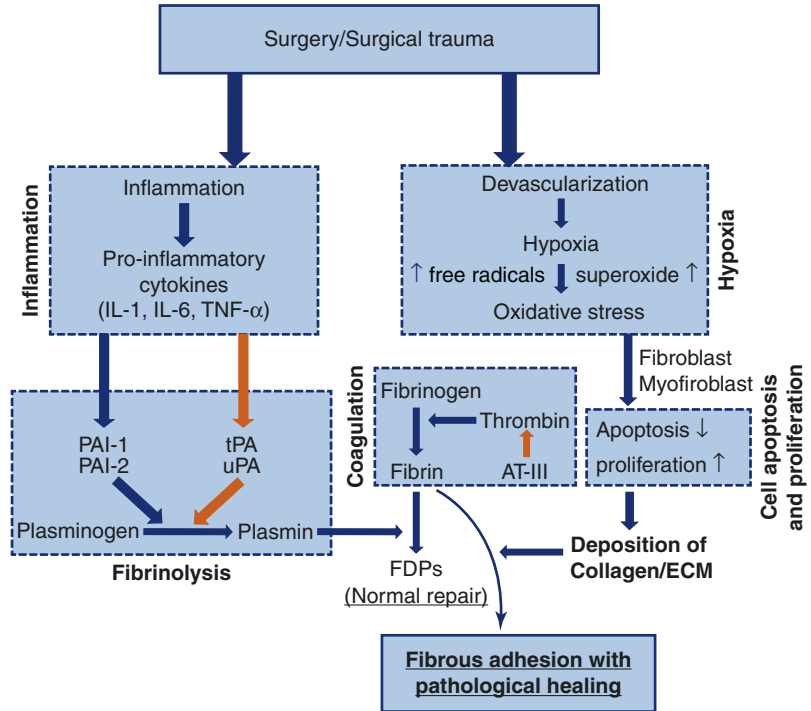
### 18.4.3 Pathophysiology

#### 18.4.3.1 Postoperative Adhesions

Aside from normal peritoneal regeneration, postoperative peritoneal adhesion formation is a healing process following any peritoneal injury or surgery [151]. The balance between fibrin deposition and degradation is crucial in determining normal peritoneal healing or adhesion formation (Fig. 18.26). When the fibrin is completely degraded, normal peritoneal healing may occur. In contrast, incompletely degraded fibrin may serve as a scaffold for fibroblasts and capillary ingrowth to form peritoneal adhesions.

Peritoneal healing differs from that of other epithelial tissues. In the healing process, the reepithelialization of peritoneal surfaces occurs simultaneously throughout the surgical site because mesothelial cells migrate into the supportive matrix and initiate multiple repair sites [159]. This contrasts with epidermal repair, which gradually heals from wound borders. The mesothelial covering of defects occurs in approximately 3 days, and complete surface repair of the peritoneum is usually completed in 5–8 days. Adhesion formation is related to suture material, tissue devascularization, ischemia, infection, the amount of manipulation, and the degree of aseptic technique [160, 161]. The normal reparative process is profoundly influenced by ischemia. As so many factors are involved in this complex process, the contribution of peritoneal closure or nonclosure to adhesion formation may be insignificant [162].

**Fig. 18.26** Balance between plasminogen activators and plasminogen inhibitors. *TIMP*: tissue inhibitors of metalloproteinases, *MMP* matrix metalloprotease, *ECM* extracellular matrix, *tPA* tissue-type plasminogen activator, *uPA* urokinase-type plasminogen, *PAI* plasminogen-activating inhibitor, *IL-1* interleukin 1, *IL-6* interleukin 6, *AT-III* antithrombin III. (Reproduced with permission from [163] under the CC BY 4.0)



#### 18.4.3.2 Gravid Uterine Enlargement

As the uterine fundus arises out of the pelvis, intraperitoneal adhesions may initially produce a partial bowel obstruction, which may become complete as the uterine bulk increases [164].

#### 18.4.3.3 Previous Appendectomy

Approximately 50% of patients with adhesive obstruction had a previous appendectomy. The technique of appendectomy or the stage of appendicular inflammation was not described. Obstruction most commonly appears during the first pregnancy after surgery for acute appendicitis. In many cases, appendectomy was performed more than 9 years before adhesive obstruction in pregnancy. The terminal ileum is the most common site of obstruction during pregnancy [157, 158] and the puerperium [155]. The obstruction of the long loop of the sigmoid colon occurred 10 years after the appendectomy [154]. A possible

explanation is sudden changes in the position of bowel loops during uterine enlargement in pregnancy or after CS or vaginal delivery. These changes cause bowel rotation around the adhesive bend(s) or kinking of the bowel.

#### 18.4.4 Prevention

These prevention strategies can be grouped into four categories: general principles, surgical techniques, mechanical barriers, and chemical agents [165].

##### 18.4.4.1 Surgical Technique

Peritoneal damage should be avoided by careful tissue handling, meticulous hemostasis, continuous irrigation and avoiding unnecessary drying, ineffective use of foreign bodies, and suturing or clamping of tissue. The use of fine and biocom-

patible suture materials, atraumatic instruments, and starch-free gloves is recommended. The use of starch-powdered gloves is associated with an increased risk of extensive postoperative peritoneal adhesions. Foreign bodies most frequently found in postoperative adhesions are surface powders from surgical gloves; lint from packs, drapes, and gowns; wood fibers from disposable paper items; and suture materials. However, in the absence of an additional peritoneal injury, foreign bodies are an infrequent cause of adhesion induction. Some intraoperative techniques, such as avoiding unnecessary peritoneal dissection or avoiding closure of the peritoneum, should be applied. Nonclosure or closure of the peritoneum did not show a difference in peritoneal adhesion formation. However, grafting or suturing peritoneal defects may increase peritoneal ischemia, devascularization, and necrosis, predisposing the site to decreased fibrinolytic activity and increased adhesion formation. Furthermore, surgical trauma should be reduced as much as possible. The surgical approach (open vs. laparoscopic) could play an important role in the development of adhesions. The laparoscopic approach results in fewer postoperative peritoneal adhesions or adhesion-related re-admissions. Adhesion formation increases with the duration of CO<sub>2</sub> pneumoperitoneum and insufflation pressure. The benefits of heated humidified CO<sub>2</sub> insufflation (37 °C and 95% relative humidity, physiological conditions) lessen adhesion formation. Furthermore, CO<sub>2</sub> pneumoperitoneum increases postoperative peritoneal adhesions in a time- and pressure-dependent relationship, and the increase is reduced by the addition of 2–4% oxygen, suggesting peritoneal hypoxia as the driving mechanism.

#### 18.4.4.2 Mechanical Barriers

Liquid or solid mechanical barriers may prevent postoperative peritoneal adhesion formation by separating peritoneal surfaces during the

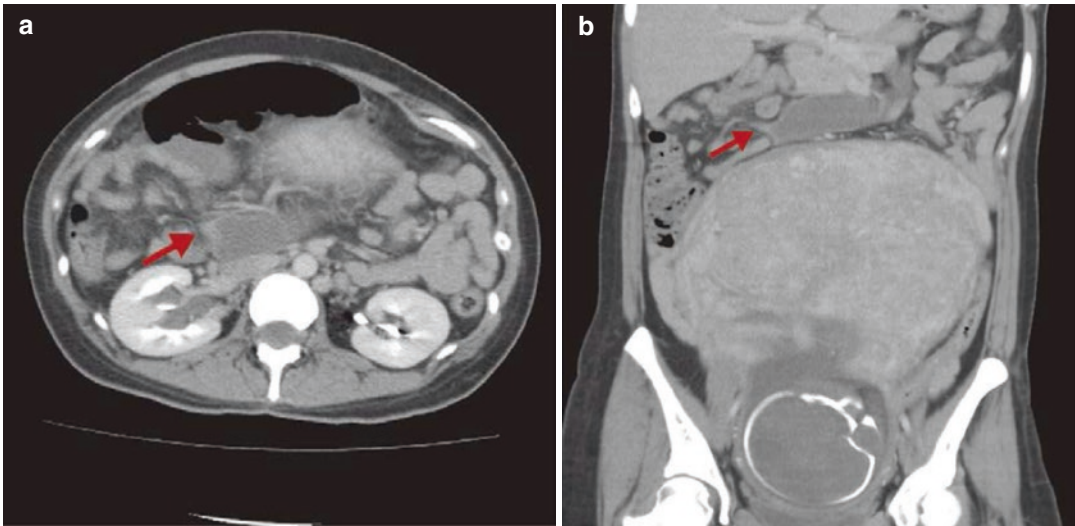
5–7 days required for peritoneal re-epithelialization. They prevent contact between the damaged serosal surfaces for the first few critical days. There are nonabsorbable and bioabsorbable films, gels, or solid membranes, but these substances did not significantly lessen postoperative adhesion formation.

#### 18.4.4.3 Chemical Agents

Chemical agents generally prevent the organization of the persisting fibrin by fibroblastic proliferation inhibition. Many agents inhibit this proliferation, such as nonsteroidal anti-inflammatory drugs, corticosteroids, calcium channel blockers, histamine antagonists, antibiotics, fibrinolytic agents, anticoagulants, antioxidants, hormones, vitamins, colchicines, and selective immunosuppressors. There was no difference and no effective clinicalness of almost all these agents. *In vitro* studies have demonstrated that vitamin E has antioxidant, anti-inflammatory, anticoagulant, and antifibroblastic effects and decreases collagen production. It is effective for reducing adhesion formation. Vitamin E, administered intraperitoneally, is as effective as carboxymethylcellulose membrane in preventing postoperative adhesions.

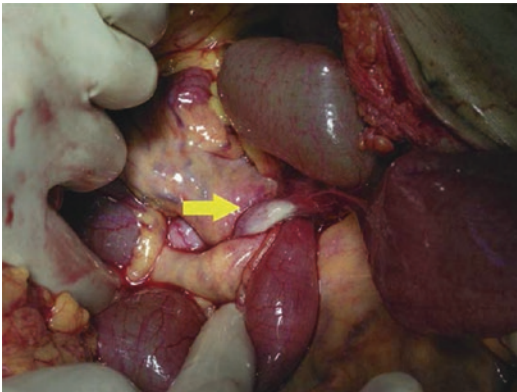
### 18.4.5 Diagnosis

Diagnostic workup is the same for every patient presenting with symptoms and signs of bowel obstruction, no matter the cause (see Sect. 18.1). Abnormal laboratory parameters with SBO were present in only 26% [166]. On plain abdominal X-rays, adhesions are not visible. Sometimes thick adhesive bands can be visualized on abdominal CT (Fig. 18.27) and confirmed intraoperatively (Fig. 18.28). The diagnosis was confirmed on US in 49%, CT in 39%, X-ray in 15%, and MRI in 14% [166].



**Fig. 18.27** (a) Axial view of upper abdominal CT scan. The bird-beak shape indicates the obstructive level of the duodenum-jejunum junction (*red arrow*). (b) Coronal view of upper abdominal CT scan. The same bird-beak

shape could be identified (*red arrow*). The distended intestine was at the proximal end. (Reproduced with permission from [167])



**Fig. 18.28** Adhesion band was identified during operation (*yellow arrow*). Above the adhesion band, the distended proximal duodenum was found. (Reproduced with permission from [167])

indicate further diagnostic workup in pregnant patients. Oral contrast media treatment with Gastrografin can be tried [168]. Conservative management was successful in only 4% [166].

#### 18.4.6.2 Surgical Treatment

Approximately 90% of SBO during pregnancy are treated surgically [168]. Emergent exploration is indicated for the following:

- Clinical deterioration,
- Unsuccessful conservative therapy (48 h),
- Suspected strangulation (clinical deterioration, the elevation of WBC, and CRP).

### 18.4.6 Treatment

#### 18.4.6.1 Conservative Treatment

Initial treatment of SBO from adhesions can be conservative. It consists of bowel rest, IV fluids, and NG tube placement. In nonpregnant patients, a plain abdominal X-ray is indicated every 6–12 h, while clinical evaluation every 6 h can

Total adhesiolysis is always performed to eliminate the possibility of postoperative bowel kinking around remaining adhesions, as in the general population. Laparoscopic surgery was performed in only 7% [166].

## 18.5 Small Bowel Volvulus

### 18.5.1 Small Bowel Volvulus

#### 18.5.1.1 Incidence

Small bowel volvulus is rare in Western countries but common in Africa, India, Nepal, and the Middle East [169–171]. It represents only 1–3% of cases of intestinal obstruction in pregnancy [172]. The major sites of volvulus are the sigmoid colon, cecum, and small bowel [173]. Small bowel volvulus, primarily secondary to malrotation, is extremely rare (see Sect. 18.5.2). Most cases of intestinal obstruction secondary to small bowel volvulus occur in the third trimester or puerperium [7, 169, 174–177]. However, cases in the first trimester were also described [178].

#### 18.5.1.2 Pathophysiology

Primary small bowel volvulus can occur without any predisposing cause. Volvulus results from the intestine rotating about its mesenteric axis, resulting in a closed-loop obstruction. Conditions implicated in the development of volvulus include adhesions, congenital bands, Meckel's diverticulum, and hernias. In advanced pregnancy, the enlarged uterus displaces the mobile cecum out of the pelvis into the right upper quadrant. The small bowel mesentery and superior mesenteric vessels become the points of rotation and torsion. However, spontaneous detorsion is restricted by the position of the gravid uterus [179, 180]. The uterus enlarges most rapidly between 16 and 20 weeks and again between 32 and 36 weeks when obstruction occurs most frequently [181, 182]. Volvulus results in partial or complete obstruction of the small intestine with proximal distension and torsion at the fixation point [6]. Torsion of the small bowel around its mesentery results in obstruction of the mesenteric blood flow. This leads to severe ischemia followed by extensive bowel infarction.

#### 18.5.1.3 Clinical Presentation

During pregnancy, intestinal volvulus can be extremely difficult to diagnose clinically, as the physical signs can be misleading and may not be those of classic bowel obstruction. Patients typically complain of severe abdominal pain that appears out of proportion to the physical signs. Clinical presentation of small bowel volvulus is due to mechanical obstruction and vascular compromise with resultant ischemic bowel. Initial symptoms are similar to those common in pregnancy, including crampy abdominal pain, nausea, vomiting, and constipation, frequently delaying definitive diagnosis. Normal or hypoactive bowel sounds may accompany persistent vomiting. Unlike intermittent, paroxysmal, regular uterine contraction pain, abdominal pain of the volvulus is ongoing and mostly epigastric. Feculent vomiting is a sign of a complete bowel obstruction. Classical findings of bowel obstruction in the nonpregnant patient, including constipation, altered bowel sounds, abdominal distension, and peritoneal signs, are frequently obscured by the gravid uterus [173, 181, 182]. When bowel ischemia ensues, hematemesis could lead to an initial diagnosis of upper gastrointestinal bleeding [183]. In advanced ischemia with bowel gangrene, there are signs of peritonism with shock.

#### 18.5.1.4 Diagnosis

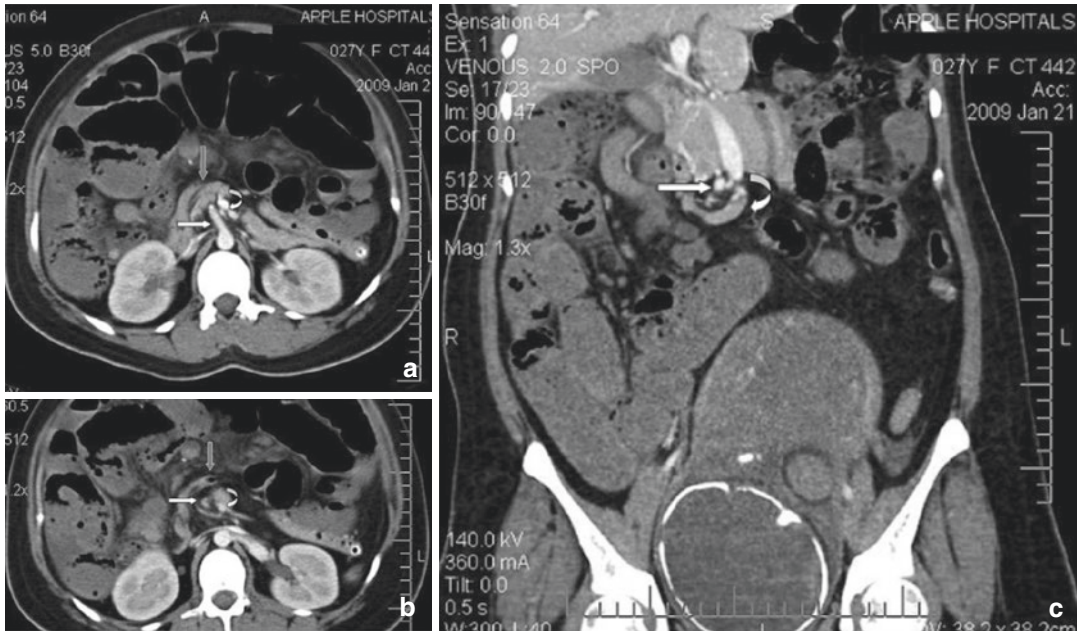
##### Transabdominal Ultrasound

The abdominal US gives information on fetal status and rules out other pathologies. Distended small bowel loops and free fluid indicate an SBO [184].

##### Abdominal CT

The evidence of volvulus on abdominal CT includes (Fig. 18.29) dilated bowel loops, intramural gas (signs of bowel ischemia), thickened bowel wall, the twisted root of the mesentery, and the *whirlpool sign* [7].





**Fig. 18.29** (a, b) Axial postcontrast CT at the level of the root of small bowel mesentery. Superior mesenteric artery (white horizontal arrow), superior mesenteric vein (curved arrow), and the twisted root of mesentery and duodenum (gray vertical arrow). (c) Coronal reconstruc-

tion of the redistribution phase shows a twisted superior mesenteric vein (curved arrow) around the superior mesenteric artery (horizontal white arrow). (Reproduced with permission from [177])

### 18.5.1.5 Treatment

Resuscitation is the principal initial treatment, including fluid replacement, electrolyte balance correction, prophylactic antibiotics, and nasogastric decompression. Treatment is always surgical, and the type of operation depends on the stage of ischemia caused by volvulus. If the bowel is vital, the cause of the volvulus is eliminated, and the bowel is detorsed to its normal position with the mesentery behind the bowel. The bowel can be ischemic but not necrotic to be detorsed and treated without resection. If the bowel is necrotic, it should be resected, and the decision to perform the anastomosis should be made. If any additional pathology could cause small bowel volvulus, it should be resected and adhesions divided if present. Some of these cases may have extensive bowel infarction, and the consequence of resection is a severe short-bowel syndrome, which would require long-term total parenteral nutrition [185–187]. If the



**Fig. 18.30** All small bowel loops are congested and infarcted due to volvulus incompatible with survival. (Reproduced with permission from [177])

complete small bowel is necrotic (Fig. 18.30), it is incompatible with survival [177]. If bowel vitality is questionable, it is left in situ, and a second look operation after 24–48 h is per-

formed [183]. With small bowel congestion during the first operation, mesenteric vein thrombosis is likely, due to mesentery torsion. Anticoagulant therapy with IV heparin is indicated. Subsequently, peroral anticoagulants should be continued for 6 months (target INR of 2.5) [183]. Laparoscopy for SBO, including volvulus, was completed in only 7% [166].

#### 18.5.1.6 Prognosis

Early diagnosis and management eliminate bowel gangrene. The bowel resection rate during the last 20 years is still high, approximately 68% [176]. The condition results in a maternal mortality rate of 3–20% and a fetal loss of 22–50% [176, 177, 188]. These numbers are higher than in the general population. Despite medical improvements, complete small bowel necrosis [177], especially if part of the large bowel is included, is incompatible with survival [189].

### 18.5.2 Congenital Intestinal Malrotation

#### 18.5.2.1 Incidence

Congenital small bowel malrotation in pregnancy is extremely rare. Only a few case reports highlight this condition in gravid patients [172, 179, 180, 190–193].

#### 18.5.2.2 Etiopathogenesis

Patients with malrotation are at an increased risk of presenting with volvulus during pregnancy due to the displacement of bowel loops by the gravid uterus. This is especially true during 16–20 weeks, 32–36 weeks, and puerperium when rapid changes in uterine size occur [179]. Volvulus results in partial SBO with proximal distension and torsion at the fixation point [6]. The issue is that the volvulus of the complete small bowel [193] or even a more extensive vol-

vulus of the small intestine, cecum, and ascending colon [191] could result in bowel necrosis incompatible with life.

#### 18.5.2.3 Clinical Presentation

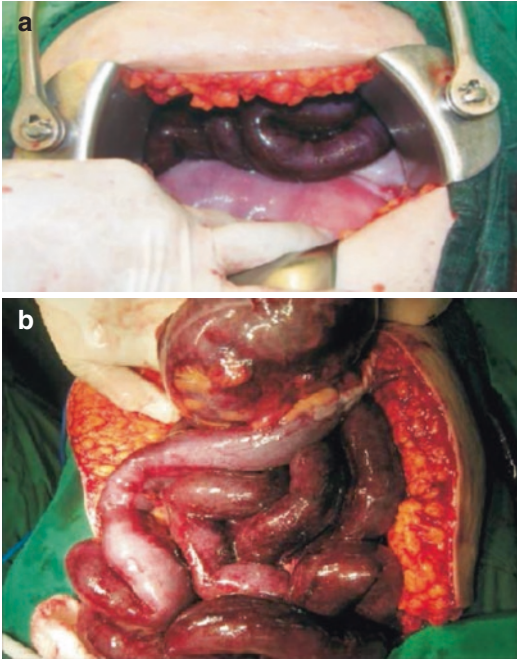
Malrotation of the midgut is common in the neonatal period while rare in adulthood. In adults, it is usually asymptomatic, with incidental discovery on imaging. Clinical presentation is the same as small bowel volvulus without malrotation (see Sect. 18.5.1.3).

#### 18.5.2.4 Diagnosis

See Sect. 18.5.1.4.

#### 18.5.2.5 Treatment

Due to the possibility of complete small bowel necrosis, emergency laparotomy is indicated if the condition is suspected to prevent bowel necrosis. Surgical resection for volvulus is the preferred treatment, as it eliminates the risk of recurrence [185]. Detorsion is an option if the bowel has not undergone necrosis and ischemia; however, a risk of recurrence remains. If the obstruction is partial, prolonged total parenteral nutrition until delivery is an option [194]. After delivery, Ladd's procedure should be performed to eliminate the possibility of midgut volvulus in subsequent pregnancies [194]. There is one case with derotation made with an enteroscope with the nasojejunal tube placement with the endoscopically proven mucosal vitality of duodenum and jejunum. This is not recommended due to several dangerous points. First, there is an increased risk of small bowel perforation while probing the abruptly short twisted segment. Second, there is an increased risk of recurrence due to the possibility of only partial derotation [172]. If gangrene of the small bowel is present (Fig. 18.31), the treatment algorithm is the same for bowel necrosis of any cause (see Sect. 18.5.1.5).



**Fig. 18.31** (a) Small intestine with the ischemic change above the uterus. (b) The ischemic intestine is due to volvulus from the proximal transverse colon, with the ischemic portion extending toward Treitz's ligament of the small intestine. The ischemic ascending colon was located in the middle of the peritoneal cavity. (Reproduced with permission from [189] under the CC BY 3.0)

### 18.5.2.6 Prognosis

The prognosis depends on the severity of bowel ischemia and the length of the bowel seized with ischemia (see Sect. 18.5.1.6).

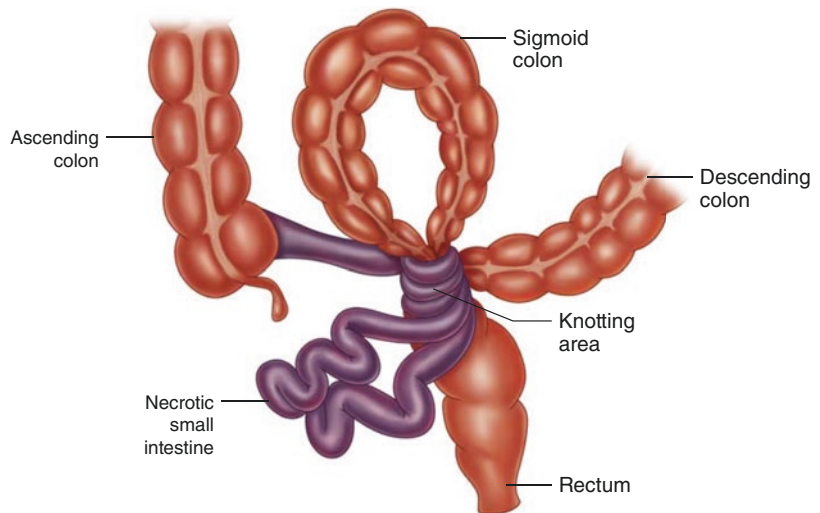
## 18.5.3 Ileosigmoid Knotting

### 18.5.3.1 Historical Perspective and Definition

Riverius first described this condition in the sixteenth century. Parker, in 1845, made the first modern report on the general population. Dunkerley reported the first case in the general population from India in 1953.

The specific type of small bowel or sigmoid volvulus is *ileosigmoid knotting* (ISK), classified into four types by Alver et al. in 1993. Type I (Fig. 18.32) is the most common one and occurs when the ileum (active component) revolves around the sigmoid colon. In type II, the sigmoid colon (active component) revolves around the ileum. In type III, the ileocecal portion revolves around the sigmoid colon. When it is difficult to determine the active or passive component, it remains undetermined or indefinite type (type IV).

**Fig. 18.32** Ileal knotting type 1. (Modified and reproduced with permission from [196])



Type I and II can be classified into subtypes of A and B depending on whether the torsion is clockwise or counterclockwise, respectively [195].

18.5.3.2 Incidence

ISK as a specific cause of small bowel volvulus and intestinal obstruction in pregnancy was present in only 15 cases between 1951 and 2014 [196–203], with an incidence ranging from 3.2 to 5.9% of all ISK cases and 12.5 to 36.4% of cases in female patients [195, 198, 204]. All patients were multiparous, almost all in the third trimester [199], with wide age distribution. It is probably underreported partly due to the published cases under other terms, such as compound volvulus, before the term, Sheperd coined ISK in 1967 [205].

18.5.3.3 Etiopathogenesis

Patients with ISK, as in other forms of small bowel volvulus during pregnancy, are at increased risk due to displacing bowel loops by the gravid uterus. This is especially true during 16–20 weeks and 32–36 weeks or puerperium from rapid changes in uterine size [179]. The problem with this entity is that volvulus of the complete small bowel [193] or even a more complex presentation with volvulus of the small intestine, cecum, and ascending colon [191] could ensue with bowel necrosis, which is incompatible with life.

Another mechanism is when a semifluid, bulky meal progresses into the proximal jejunum. It increases the mobility of the intestine, and the heavier segments of the proximal jejunum fall into the left lower quadrant. The empty loops of the ileum and distal jejunum twist in a clockwise rotation around the base of a narrow sigmoid colon. Further peristalsis forms an ISK with two closed-loop obstructions—one in the small bowel and the other in the sigmoid colon [198]. Both the ileal loops and the sigmoid colon become distended. As the knot tightens, a double-loop obstruction may progress to gangrene. The presence of elongated ileum and sigmoid colon and the presence of a narrow base with an elongated mesentery have been held responsible for the anatomical pathology of the disease. Rapid uterine shrinkage after delivery and sudden changes in the position of the abdominal organs might induce this condition. Sometimes it cannot be

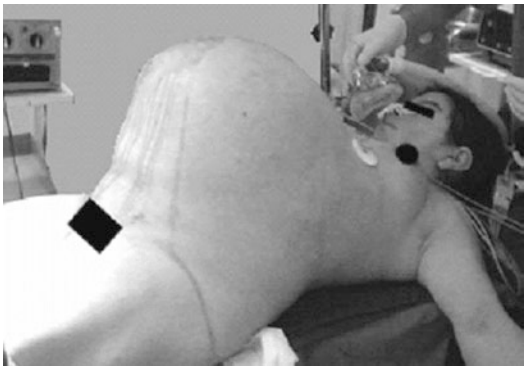
established whether ileal knotting triggered labor or labor-triggered ileal knotting [196]. Risk factors are presented in Table 18.4.

18.5.3.4 Clinical Presentation

The typical triad of ISK is intermittent abdominal pain progressing to constant pain increasing in severity, asymmetrical abdominal distention (Fig. 18.33), and absolute obstipation [199]. Additional symptoms include nausea and vomiting, and other signs may include hyperkinetic or hypo/akinetic bowel sounds, empty rectum, fever, and dehydration. A striking feature of ISK is rapid deterioration [206]. Muscular guarding with rebound tenderness and melena suggests

**Table 18.4** Risk factors for ileosigmoid knotting in pregnancy

|                                        |
|----------------------------------------|
| <i>Bulky single daily meal</i>         |
| Eating habit                           |
| Ramadan fast                           |
| Morning sickness                       |
| <i>Anatomic factors</i>                |
| Long small bowel mesentery             |
| Hypermobile small bowel                |
| Long sigmoid colon on a narrow pedicle |
| Relaxed anterior abdominal wall        |
| <i>Pregnancy</i>                       |
| Multiparous                            |
| 32–36 weeks                            |
| Puerperium                             |
| <i>Adhesions</i>                       |
| <i>Meckel’s diverticulum</i>           |
| <i>Internal herniations</i>            |
| <i>Bowel malrotation</i>               |



**Fig. 18.33** Asymmetrically, atypically distended abdomen appeared after delivery and again at puerperium. (Reproduced with permission from [196])



peritonitis or bowel gangrene. The clinical appearance of ISK in pregnant women is not distinctive from the presentation in nonpregnant females [199, 204]. The mean duration of symptoms is shorter for pregnant women than for nonpregnant female patients, but the difference is not statistically significant (36.0 h vs. 46.8 h) [199].

### 18.5.3.5 Diagnosis

Recent preoperative diagnostic accuracy of ISK in pregnancy is 14% due to infrequency and atypical radiographic findings [203]. A common preoperative diagnosis in pregnancy is intestinal obstruction, mainly colonic volvulus [206].

#### Plain Abdominal X-Ray

The key radiological features on plain abdominal X-rays of ISK consist of a dilated loop of the sigmoid colon, evidence of small intestinal obstruction, and retention of feces in an undistended proximal colon (Fig. 18.34). The dilated loop usually lies on the right side of the abdomen, and the limbs taper inferiorly into the right lower quadrant. Medial deviation of the distal descending colon is an inconsistent but highly specific finding [207]. Probably these classic findings are not commonly present during pregnancy due to the distorted anatomy, especially in advanced pregnancy when ISK is more common.



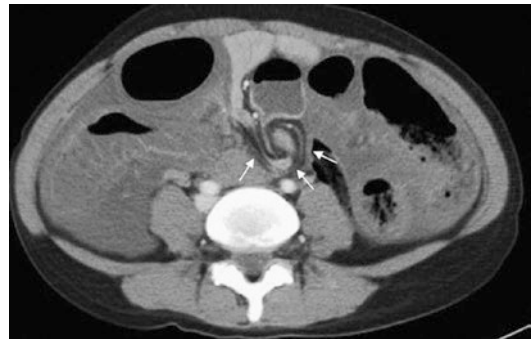
**Fig. 18.34** Plain abdominal X-ray reveals a sigmoid colon loop (white arrows) in the mid-abdomen with air-liquid levels of small bowel around the sigmoid colon base. (Reproduced with permission from [203] under the CC BY 3.0)

#### Transabdominal Ultrasound

The abdominal US may give information about the fetus and rule out other pathologies. Distended loops with thickened bowel walls are visualized. Further diagnosis information with US is rarely informative.

#### Abdominal CT

Despite the high diagnostic rate in the general population [208, 209], CT is rarely used in pregnancy. It demonstrates a twisted and dilated sigmoid colon with whirled mesentery and twisted and dilated small intestinal segments (Figs. 18.35 and 18.36).



**Fig. 18.35** Contrast-enhanced CT (axial view) shows a dilated loop of the intestine with a surrounding whirl (white arrows). (Reproduced with permission from [203] under the CC BY 3.0)



**Fig. 18.36** Contrast-enhanced CT (coronal view) shows a dilated loop of the sigmoid colon in the right lower abdomen with whirling of the sigmoid mesocolon and mesenteric root, suggestive of strangulation. Dilated loops of the small bowel are concentrated in the upper left abdomen. (Reproduced with permission from [203] under the CC BY 3.0)



### 18.5.3.6 Treatment

Due to the possibility of complete small bowel necrosis, emergency laparotomy is indicated if the condition is suspected to prevent bowel necrosis. Surgical resection for volvulus is the preferred treatment [185]. If the small intestine and sigmoid colon are gangrenous, then ileal resection with primary anastomosis and sigmoid resection with Hartmann's procedure is performed. If the only ileum is gangrenous, it is resected, and primary anastomosis is made. Due to the high incidence of recurrent (isolated) sigmoid volvulus (in both general and pregnant populations) [185, 210, 211], it should be resected even if vital and Hartmann's procedure performed (see Sect. 18.8.5).

Detorsion (with sigmoidostomy or sigmoido-pxy) is an option if the bowel has not undergone necrosis and ischemia. However, the risk of recurrence remains. It is used to shorten the operation in an unstable patient. Because untwisting the knot is difficult and risks toxin release and perforation, it has been advised that the sigmoid colon is deflated using needle deflation or colotomy, or *en bloc* resection of the gangrenous colon.

If the obstruction is partial, prolonged total parenteral nutrition until delivery is an option [194]. After delivery, Ladd's procedure should be performed to eliminate the possibility of midgut volvulus in subsequent pregnancies [194]. There is one case with derotation made with an enteroscope with the nasojejunal tube placement with the endoscopically proven mucosal vitality of the duodenum and jejunum. This is not recommended for several reasons. First, there is an increased risk of small bowel perforation while probing the abruptly short, twisted segment. Second, an increased risk of recurrence is due to the possibility of partial derotation [172].

### 18.5.3.7 Prognosis

In the general population, the mean mortality rate of ISK is 6.8–8% with nongangrenous and 20–100% with gangrenous bowel [212]. Although the mortality and morbidity rates when ISK was the cause of small bowel volvulus were higher in pregnant patients, the differences were not statis-

tically significant (33.3% vs. 18.8%). The mean hospitalization stay was longer for pregnant patients than nonpregnant female patients (15.5 days vs. 10.8 days) [199]. Recent mortality is 57% [203].

## 18.6 Colorectal Carcinoma

### 18.6.1 Historical Perspective

Many reports of colorectal carcinoma (CRC) during pregnancy appear in the literature, the first being in 1835, and Cruveilhier (Fig. 18.37) reported the first rectal carcinoma in pregnancy in 1842. Evers reported the first case of colon cancer above peritoneal reflection in 1928 [213]. These early reports were concerned mainly with the obstetric problems of delivering the fetus in the presence of a pelvic tumor. Robert Greenhalgh (St. Bartholomew's Hospital; consulting physician to the Samaritan Hospital for Women and City of London Lying In Hospital) in 1866 described a CS done under



**Fig. 18.37** Jean Cruveilhier (1791–1874), Centenaire de la Faculté de Médecine de Paris. Portrait from 1837. (From Wikipedia [216])

an ether spray on a woman with obstructed labor from a rectal carcinoma [214]. Interest in this subject lies in two effects, that of the pregnancy on the CRC and that of the complications of the CRC on the pregnancy management. Warren, in 1957, concluded that pregnancy does not adversely affect the course of carcinoma of the rectum [215].

## 18.6.2 Incidence

Only 2–6% of CRC is found before the age of 40, which is a period of reproductive age [217]. However, CRC in pregnancy is uncommon, with a reported incidence of 0.002–0.1% [217–221], which rises with age. CRC represents 4.1% of all cancers during pregnancy and the first postdelivery year [222]. Nijhoff (*Groningen, Netherlands*), in 1905, collected twenty-two published cases [223]. Until 1949, 75 cases were published [224, 225]. Over 300 cases of CRC associated with pregnancy have been reported until 2015 [226–229]. The first two published cases of perforated low rectal and sigmoid cancer were by Nash in 1967 [230]. Both cases were in the third trimester. Most cases of CRC are discovered in late pregnancy, and 60–80% of the patients have rectal carcinoma [231]. The tumor distribution includes the right colon in 7.3%, transverse colon in 4.9%, left colon in 4.9%, sigmoid colon in 19.5%, and rectum in 63%. Dukes' stage at presentation was A, 0%; B, 39%; C, 41%; and D, 15% [228]. Most patients are diagnosed postpartum (76.8%), whereas only 20.9% before delivery and 2.2% at delivery [219].

Pregnant women have a much higher incidence of rectal cancer (83%) than colonic sites (17%). This is in contrast to nonpregnant women younger than 40 years, among whom the site distribution is 68% colon and 32% rectum, respectively [232].

## 18.6.3 Carcinogenesis and Risk Factors

### 18.6.3.1 Hormonal Receptors

Estrogen receptors (ER) and progesterone receptors (PgR) [233] may be involved in the pathogenesis of CRC during pregnancy. As many as 20–54% of colon tumors have ERs [234], and 42.8% have PgRs [235]. These findings suggest that increased levels of estrogen and progesterone found in pregnant women could stimulate the growth of CRCs with these receptors. Stimulating these receptors could also help explain the advanced stages found in most patients at the time of diagnosis. However, the data to support the role of these receptors in the pathogenesis of CRC are scarce, and conflicting data exist regarding ERs and PgRs in CRC. One study claims no ER+ and almost no PgR+ (1/156) tumors in women diagnosed with CRC [234].

### 18.6.3.2 Cox-2 Enzymes

Cox-2 products appear to be essential for the early pregnancy sequences, including ovulation, fertilization, implantation, and decidualization [236]. The early events of pregnancy and the pathogenesis of tumor spread have important similarities. Both events require cells to migrate from the site of origin to another site at which these cells must establish new vasculature to grow and mature [236]. Cox-2 enzymes have high levels in many CRC cells [237]. Cox-2 inhibitors such as aspirin can alter the course of CRC [237]. Increased levels of Cox-2 enzymes in pregnant patients could play a role in the pathogenesis and prognosis of CRC in pregnancy. However, no studies have been performed to explore this potential relationship [227].

### 18.6.3.3 Other

CRC is a rare event in young patients. This implies that predisposing factors likely cause CRC in pregnancy among this population of patients compared with the general population of patients with CRC.

Parity is neither positively nor negatively associated with CRC [219].

Increasing age is associated with an increased risk for CRC development, with a small number of cases in women less than 30 years old [220, 238, 239].

Predisposing factors for CRC include hereditary nonpolyposis CRC (i.e., Lynch syndrome), familial adenomatous polyposis, Gardner's syndrome, Peutz–Jeghers syndrome, and inflammatory bowel disease [227]. However, these increased risk groups represent only a small portion of CRCs diagnosed in pregnancy [226]; around 21% of pregnant patients with CRC had these strong predisposing factors [221]. The presence of genetic abnormalities is not known. Family history must be recorded, and evaluation by genetic cancer clinics should be considered [227].

In countries fortifying flour with folic acid, a steady decrease in neural tube defects (NTDs) has been documented [240]. The main criticism against flour fortification has been that this strategy exposes large segments of the population, such as those who never become pregnant, to folate levels beyond necessary [241]. In parallel to the reports on a dramatic decrease in rates of NTDs in jurisdictions where fortification took place, concerns have been raised that heightened folate status may increase the risk of cancer in general, with CRC on the top [242]. A high folate level decreases CRC risk between 8–15% [243] and 19–25% [244]. Women of reproductive age should not be discouraged from an adequate folate intake based on a wrongly perceived risk of CRC.

## 18.6.4 Clinical Presentation

*Any excessive enlargement of the abdomen or the appearance of pressure symptoms should always lead one to make a careful examination, and in not a few cases, a tumour will be found occupying the pelvic cavity.*

(John Whitridge Williams, 1903)

### 18.6.4.1 Elective Presentation

The most common clinical manifestations of CRC include nonspecific, vague abdominal pain, nausea, vomiting, weight loss, change and irregularity in bowel habits, and rectal bleeding. Some of these symptoms are common in pregnant patients and are considered the usual manifestations of pregnancy without an appropriate evaluation [227, 245]. The delay in initiating the workup for the symptoms related to CRC is one of the major contributing factors to the poor prognosis [246]. In general, pregnant women gain weight. However, women can experience weight loss in the first trimester due to nausea and hyperemesis gravidarum. On the other hand, pregnancy can obscure weight loss secondary to CRC in the second and third trimesters. Rectal bleeding is a common finding during pregnancy and is usually secondary to the high incidence of external and internal hemorrhoids; however, rectal bleeding is a particularly ominous sign and should never be attributed solely to pregnancy itself without a proper evaluation. It is highly suspicious if [1] the fresh blood is mixed with stool, [2] if a large amount of mucus is present, [3] old blood is found, or [4] if unexplained diarrhea, with or without blood, is evident. With these symptoms, a digital rectal examination and anoscopy are mandatory. Nausea and vomiting are common pregnancy symptoms, particularly during the first trimester. Constipation often accompanies pregnancy, which can delay workup for CRC. Abdominal mass constitutes a natural process in pregnancy. Potential palpable masses secondary to CRC are often missed, especially in advanced pregnancy. A Krukenberg tumor from primary CRC can result in virilization—facial hirsutism, deepening voice, facial acne, and clitoromegaly [247].

Warning symptoms and signs help make the diagnosis at an early stage of the disease (Table 18.5).

**Table 18.5** Commonly confusing signs, symptoms, and laboratory results between normal pregnancy and colorectal cancer

| Signs, symptoms, and lab | Normal pregnancy                                                                   | Pregnancy with colorectal cancer                                                          |
|--------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| Weight loss              | In general, weight gain, but women can experience weight loss in the 1st trimester | Pregnancy can obscure weight loss secondary to CRC, primarily in 2nd and 3rd trimesters   |
| Rectal bleeding          | Common in pregnancy secondary to the high incidence of hemorrhoids                 | Often attributed to hemorrhoids without pursuing an appropriate workup                    |
| Nausea and vomiting      | Common in pregnancy, particularly during 1st trimester                             | Often attributed to pregnancy, delaying workup                                            |
| Constipation             | Common in pregnancy                                                                | Often attributed to pregnancy, delaying workup                                            |
| Abdominal mass           | A natural process in pregnancy                                                     | Potential palpable masses secondary to CRC often missed secondary to changes in pregnancy |
| Anemia                   | Physiologic findings in pregnancy                                                  | Anemia of pregnancy masks blood loss from CRC                                             |

Reproduced with permission from [226]

**18.6.4.2 Emergent Presentation**

Emergent presentation is mostly intestinal obstruction, which can lead to bowel perforation due to distension and ischemia. Another possibility is tumor perforation. Due to CRC, intestinal obstruction presents with new-onset (profound) vomiting, sometimes feculent. Patients have severe abdominal pain, which is colicky at the beginning and then constant with significant abdominal distension during the short period despite the trimester of pregnancy. There is an absence of stool and, more importantly, flatus. The presentation of perforated CRC is sudden and severe pain. With bowel or CRC perforation, signs of peritonism can be elicited. In the underlying state is bowel obstruction, and abdominal distension precedes signs of peritonitis.

**Table 18.6** Differential diagnoses and causes of colorectal obstruction in pregnancy

| Differential diagnosis | Cause of obstruction |
|------------------------|----------------------|
| Hyperemesis gravidarum | Endometriosis        |
| Gastroenteritis        | Adhesions            |
| Threatened labor       | Volvulus             |
| Constipation           | Intussusception      |
| Mesenteric ischemia    |                      |

**18.6.5 Differential Diagnosis**

In early pregnancy, a bowel obstruction can initially be confused with hyperemesis gravidarum. The difference is found during the examination of the abdomen. When large bowel obstruction is present without a competent ileocecal valve, feculent vomiting is present with significant distension of the abdomen. There is no passage of flatus and stool, while bowel habits during hyperemesis gravidarum are normal. Sometimes, in advanced pregnancy, the clinical presentation is attributed to threatened labor [248]. Diagnostic delay in a patient with virilization due to the Krukenberg tumor is more pronounced with a prepregnancy diagnosis of polycystic ovary syndrome [247]. New-onset virilization, especially with other symptoms, such as (new-onset) obstipation or (new-onset) rectal bleeding, should raise suspicion of CRC. Differential diagnoses are presented in Table 18.6.

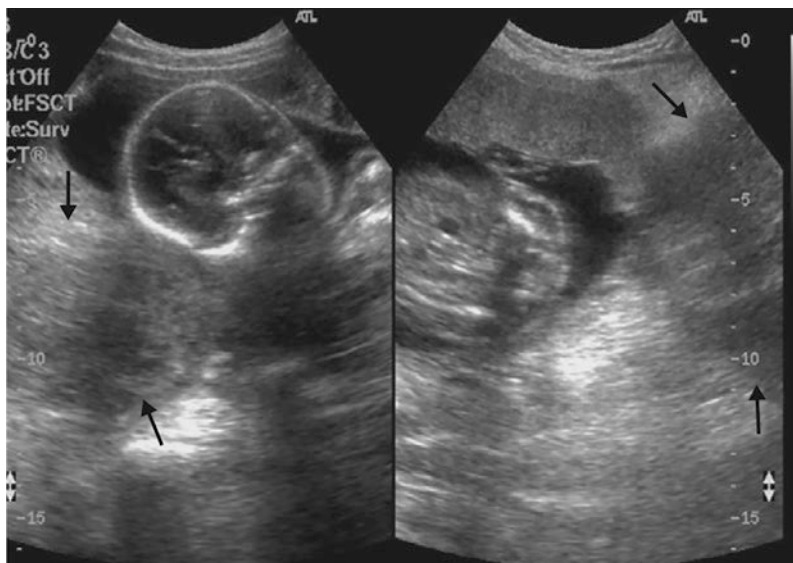
**18.6.6 Diagnosis**

**18.6.6.1 Laboratory Findings**

The serum carcinoembryonic antigen (CEA) levels are normal or marginally elevated in normal pregnancy [226, 245]. The CEA levels should, therefore, be measured and used in the same way as in nonpregnant patients [245]. Although the CEA level is not useful as a screening test for CRC because of its low sensitivity and specificity, preoperative testing is useful in determining the prognosis and providing a baseline for comparison with postoperative levels. Anemia is a physiological finding in pregnancy. Therefore, lower hemoglobin levels are not diagnostic, but microcytic anemia or low iron levels should raise

**Fig. 18.38**

Ultrasonogram shows the fetus and two ovarian masses (*black arrows*). (Reproduced with permission from [250])



suspicion of bleeding, not the dilution of pregnancy [248]. In such cases, a fecal occult blood test is mandatory.

With CRC perforation, laboratory findings show elevated levels of WBC and CRP. Prerenal insufficiency is due to the shift of fluid in the third space.

#### 18.6.6.2 Plain Abdominal X-Ray

In the elective presentation, a plain abdominal X-ray has no diagnostic value. In the emergent presentation, a plain abdominal X-ray confirms the colorectal level of obstruction with air–liquid levels. A plain abdominal X-ray shows pneumoperitoneum (gas under the diaphragm dome) if the perforation is above the peritoneal fold.

#### 18.6.6.3 Transabdominal Ultrasound

The abdominal US rarely defines primary CRC but can show liver metastases as an indirect clue to the diagnosis. Ovarian metastatic disease from CRC poses another diagnostic challenge. The incidence of ovarian metastases from CRC (Krukenberg tumor) is higher in pregnant (25%) than in nonpregnant (3–8%) patients [246, 249]. It could mislead the clinician into diagnosing primary ovarian tumors preoperatively (Fig. 18.38) with a false diagnosis of external colon compression from ovarian tumors.



**Fig. 18.39** Pretreatment T2 weighted sagittal view MRI of the pelvis shows thickening of the anorectum 1.2 cm from the anal verge and extending 4.2 cm craniocaudally. The uterus is anteverted with a gestational sac. (Reproduced with permission from [251] under the CC Attribution License)

#### 18.6.6.4 Abdominal MRI

MRI is the most accurate diagnostic imaging modality for CRC in pregnancy. It accurately defines the location and extent of rectal carcinoma (Fig. 18.39). Also, metastatic CRC can be delineated as a Krukenberg tumor. Hepatic





**Fig. 18.40** Coronal abdominopelvic CT shows colonic distention with abrupt transition to complete collapse in the region of the sigmoid colon (*blue arrow*) and gravid uterus (*red arrow*). (Reproduced with permission from [252] under the CC BY 4.0 Attribution License)

metastases, the most common metastatic disease of CRC, are common with Krukenberg tumors during pregnancy.

#### 18.6.6.5 Abdominal CT

In emergency settings, CT is more commonly used. The location of colon obstruction is commonly visualized (Fig. 18.40).

### 18.6.7 Treatment

#### 18.6.7.1 Surgical Treatment

##### Elective Surgery

Nijhoff, in 1905, held that as the child is not viable, the operator must choose between terminating the pregnancy and waiting until the child is viable. He advocated the former procedure, believing that waiting for an operable tumor might be allowed to become inoperable [223].

Oncologic resection is recommended if the tumor is resectable, especially in <20 weeks of gestation. After 20 weeks of pregnancy, surgery should be delayed for a reasonable maturation of the fetus (32 weeks). After 32 weeks, CS is recommended after documentation or stimulation of fetal lung maturity with concomitant tumor resection [219, 220]. It can be done in a single act or as a two-stage procedure [227]. In the first stage, delivery is performed. After 2–3 weeks, when the uterus returns to normal size and the pelvic venous congestion related to pregnancy decreases, oncologic resection of the CRC is performed. CRC surgery is done in one stage after an uncomplicated CS [245].

In advanced stages, when adjuvant therapy is needed, elective abortion would help to save a mother's life. In advanced pregnancy, it is possible to pursue adjuvant therapy after early delivery. In religious countries like Iran, there is another extra challenge for parents and clinicians since, due to religious beliefs, legal abortion is only permitted up to week 16. After this time, there would be problems performing the abortion legally.

When faced with malignant bilateral ovarian tumors, the ideal surgical approach is a total hysterectomy, bilateral salpingo-oophorectomy, pelvic and abdominal washings, omentectomy, and para-aortic lymph node biopsies. However, even in bilateral malignant disease, a hysterectomy can be omitted if the uterus is not grossly involved, thus allowing the preservation of an existing pregnancy. Macroscopic ovarian metastases from primary CRC are present in 3.4–5.4% of the general population [253]. No guidelines exist for prophylactic oophorectomy for the prevention of metachronous ovarian metastases. Surgical and adjuvant treatments have obvious implications for women of childbearing age.

##### Emergency Surgery

The first two published cases of perforated low rectal and sigmoid cancer were by Nash in 1967 [230]. Nash defined two possible plans of action: If the pregnancy is sufficiently advanced, labor can be induced, the uterus emptied, and the colonic condition is treated in much easier oper-

ating conditions. If, however, the patient's condition is too poor or if she is not yet at full term, the operation must be done in the presence of the gravid uterus. In these circumstances, resection is very difficult, and exteriorization is the only possible treatment.

### 18.6.7.2 Conservative and Bridge Therapy

Along with surgery, other approaches to relieve bowel obstruction should be considered. Retrograde insertion of a colonic stent in the general population has been used to relieve a colonic obstruction caused by malignancy [246]. Colonic stent decompression is palliation for the widespread metastatic disease or serves as a bridge to surgery but at the risk of greatly increased maternal and fetal morbidity [7].

### 18.6.7.3 Mode of Delivery

*In rare instances, malignant tumors of the rectum may so obstruct the pelvic canal as to render Cesarean section imperative.*

(John Whitridge Williams, 1903)

The mode of delivery should not be affected by cancer, except for a CS owing to a distal tumor obstructing the birth canal or anterior rectal wall carcinoma. Unfortunately, pregnancy-associated cases of CRC have higher rates of CS and preterm deliveries. Preterm deliveries are not only secondary to scheduled inductions and CS-related to the cancer diagnosis but also have higher rates of preterm labor [219]. The placenta should be examined for metastases [246]. In cases with stercoral peritonitis, CS via an infected peritoneal cavity seems very unwise and would appear to be indicated if a perforated CRC obstructs vaginal delivery.

### 18.6.7.4 Chemotherapy

Adjuvant chemotherapy with *5-fluorouracil* (5-FU) is suggested for stage III CRC; however, the risk and benefits should be discussed with the patient [245]. The most severe complications occur when the chemotherapy is given during

3–12 weeks of gestation [254]. Mechanisms by which 5-FU may lead to fetal abnormalities include interrupting DNA synthesis and cell development by inhibiting embryonic thymidylate synthase [255]. During the first trimester, 5-FU has been associated with spontaneous abortion and normal-term births [256, 257]. Moreover, no congenital anomalies or clinically significant adverse effects were observed in infants whose mothers were treated for breast cancer during the second and third trimesters of pregnancy with IV 5-FU combined with doxorubicin, cyclophosphamide, and other chemotherapeutic agents [258]. There are no reports on the use of 5-FU during lactation.

*Cisplatin* and other platinum-based chemotherapy drugs are not recommended during pregnancy or breastfeeding [259]. Studies in animals have shown that oxaliplatin causes miscarriages, decreased weight or death of the fetus, and problems with bone formation [260]. Patients should use some kind of birth control while receiving oxaliplatin, and a pregnancy test should be performed before chemotherapy. Some recommend lower doses of chemotherapy during pregnancy because of the higher concentration of the free chemotherapeutic agent in a pregnant woman compared with nonpregnant women [261]. In addition to the dose reduction, within 3 weeks of anticipated delivery or beyond 35 weeks of gestation, it should not be administered to avoid transient neonatal myelosuppression and potential complications such as bleeding, sepsis, and death at the time of delivery [262]. In five published studies of 11 patients treated with combination chemotherapy, including cisplatin for cervical cancer in pregnancy, neonatal development was normal [263]. It is unknown whether this drug passes into breast milk.

*Irinotecan* was approved as part of a first-line treatment regimen containing 5-FU and leucovorin for metastatic CRC. It significantly improved objective tumor response rates, time to tumor progression, and survival compared with 5-FU and leucovorin alone [264]. Irinotecan is a US FDA pregnancy class D drug, meaning that human data show risks, but the potential benefit

may outweigh the risks. It may cause harm to the fetus when given during pregnancy [265]. Radiolabeling studies have shown that  $^{14}\text{C}$ -irinotecan crosses the placenta of rats after IV administration. Irinotecan administration during rat organogenesis is embryotoxic by increased postimplantation loss and decreased numbers of live fetuses. Teratogenic effects included a variety of external, visceral, and skeletal abnormalities. Irinotecan administered to pregnant rats after organogenesis through weaning caused decreased learning ability and decreased female body weights in the offspring. Irinotecan is excreted in breast milk, and breastfeeding is not recommended during therapy. The mean terminal elimination half-life for its longest-acting active metabolite, 7-ethyl-10-hydroxycamptothecin, is 10–20 h, meaning that breastfeeding should be safe after at least 1 week after treatment. There are two case reports using irinotecan (plus 5-FU and leucovorin): first at 18 weeks and the other at 23 weeks of pregnancy without harmful effects on the neonate/infant [266, 267].

Chemotherapy is safer during the second and third trimesters of pregnancy, although with an increased rate of intrauterine growth, retardation, and prematurity [268]. Fetal growth could also be affected by maternal nutritional deficiencies and anorexia induced by chemotherapy and the tumor [259]. Although a few cancer chemotherapy studies have failed to show adverse effects in treatment in the third trimester, the possible neurocognitive effect of chemotherapy cannot be excluded because brain development is not completed during pregnancy or even early in life [269]. The evidence indicates that neoadjuvant chemotherapy in pregnant women with metastatic rectal cancer spares the fetus, although it is not curative for mothers [229, 270–274].

#### 18.6.7.5 Radiotherapy

Pelvic radiotherapy is not recommended during pregnancy and is contraindicated during organogenesis because it is associated with embryonic or fetal death, malformation, and growth retardation [275]. A medical physicist should measure fetal radiation exposure during pregnancy [276]. Women with pregnancy-associated CRC were

less likely to receive chemotherapy but more likely to receive radiation than aged-matched, nonpregnant women. However, the differences in rates of adjuvant radiotherapy were not statistically significant [219]. Because most women were diagnosed after delivery, this phenomenon cannot be fully explained by a concern for the fetus unless it represents a breastfeeding concern. Future fertility should be considered before treatment because radiotherapy can cause permanent damage to the ovaries and lead to infertility [277]. No studies elaborated on the timing of radiation and chemotherapy relative to surgery, so no conclusions can be made.

#### Ovarian Transposition

The primary benefit of ovarian transposition is preventing or delaying premature menopause, not the preservation of fertility. “Curative” doses in the range of 8500 cGy with external beam plus intracavitary brachytherapy, endometrial damage essentially precludes successful pregnancy, either spontaneously or in vitro. Several authors have determined and reported the dose of radiation delivered to the ovary after successful laparoscopic oophoropexy. Covens et al. [278] studied three patients in whom ovarian transposition was performed and determined the radiation dose expected to be received by the ovaries after delivery by either an external beam radiation dose of 4500 cGy or via brachytherapy. The mean dose of radiation received by the transposed ovary was 175 cGy (range, 40–370 cGy) after a mean follow-up of 2 years. The iatrogenic menopause rate was 10%, but iatrogenic menopause did not occur in patients younger than 40.

Numerous studies have attempted to specify *radiation therapy tolerance doses* for the various tissues and structures of the body. Common dose definitions used to describe various tissue tolerances are the minimal tolerance dose, TD 5/5, and the maximal tolerance dose, TD 50/5, which refer to a severe complication rate of 5 and 50%, respectively, with 5 years of radiation completion. For the ovary, these values are approximately 300 cGy and 1200 cGy, with sterility being the endpoint of severe complication. Tolerance doses for other tissues are

significantly higher. In clinical practice, however, the tolerance doses for the ovary and other tissues may be lower, given the now common treatment regimens that typically include chemotherapy or altered radiation fractionation schemes. In general, if the ovaries can be shielded from the direct radiation beam via an oophoropexy maneuver, a dose below the TD 50/5 (300 cGy) can be achieved with a reasonable expectation of ovarian function preservation posttreatment. The rule of thumb for radiation and ovarian function could be applied, meaning 10 cm distance to the radiation field = 10% radiation dose [279].

The typical outcome measure in ovarian transposition following radiation therapy is ovarian function. This is often measured by quantitative analysis of ovary-stimulating or ovary-producing hormones and fertility outcomes. Spontaneous pregnancies are possible if the tubal function is preserved as part of the oophoropexy. Morice et al. [280] reported 37 consecutive cases of ovarian transposition. In these cases, 43% of pregnancies occurred spontaneously; of these, 75% did not have the ovaries repositioned from the adnexa. Quantitative analysis of ovarian function has been reported by Covens et al. [278] in three patients undergoing ovarian transposition. Serum FSH was normal in 67% (2/3) of patients regularly menstruating 24–32 months after radiation. Treissman et al. [281] reported on a patient with laparoscopic ovarian transposition before definitive treatment for anal carcinoma. Tulandi and Al-Took [282] reported that normal menstruation returned after irradiation in a 34-year-old woman who underwent laparoscopic ovarian transposition before radiation to treat rectal carcinoma. Although postmenopausal symptoms and elevated serum gonadotropins initially indicated ovarian failure, normal menstruation resumed and correlated with normal FSH levels 8 months after treatment. The timing depends on the treatment algorithm of rectal cancer. If the operation is indicated, it can be performed during that operation for rectal cancer. If neoadjuvant chemoradiotherapy is indicated, then laparoscopic transposition can be performed before neoadjuvant chemoradiotherapy.

Preservation of ovarian function by laparoscopic transposition of the ovaries before pelvic irradiation is a safe and effective procedure for Hodgkin's disease and various gynecologic malignancies. Historically, surgical exploration of the abdomen or pelvis as part of staging or resection procedures has allowed access to the ovaries for direct-open transposition of ovaries for planned subsequent radiation therapy.

Techniques for ovarian transposition using a laparoscopic approach vary according to the radiation field shape, size, and location. The rule of thumb for radiation and ovarian function means 10 cm distance to the radiation field = 10% radiation dose.

#### Medial Ovarian Transposition

Two options include [1] medial transposition of the ovaries behind the uterus (to lie beneath an external midline block) and [2] a superior transposition to the level of the iliac crest [283]. The disadvantage of the midline oophoropexy is a higher level of internal radiation scatter, as the area is generally surrounded by in-field radiation.

#### Lateral Ovarian Transposition

Lateral transposition includes ovarian transposition to the paracolic gutters before radiation for gynecologic malignancies [280]. This procedure is a safe and effective method of preserving ovarian function. The peritoneum of both pelvic sidewalls is incised, and the retroperitoneal spaces are opened. The common, external, and internal iliac vessels are identified. The ovarian vessels and ureters are traced on both sides. Under the direct vision of the ureters, the utero-ovarian ligaments are separated with an endoscopic linear cutting stapler. The peritoneum under and lateral to the ovarian vessels is incised to an area outside the pelvis, under direct vision of the ureters. At this point, the ovarian vessels could be turned laterally with a sufficient angle to maintain an appropriate blood supply. In three points, the ovaries and tubes are fixed high in the paracolic gutters, below the spleen and the liver, with 2-0 silk sutures to prevent torsion. The upper and lower poles of the ovaries are marked with hemo-

clips. At the end of the procedure, the adequate blood supply to both ovaries is confirmed by a small incision of the fallopian tubes, which is cauterized. The metal clips around the ovaries help verify that they would be out of the radiation portals on radiation verification films [279].

## 18.6.8 Prognosis

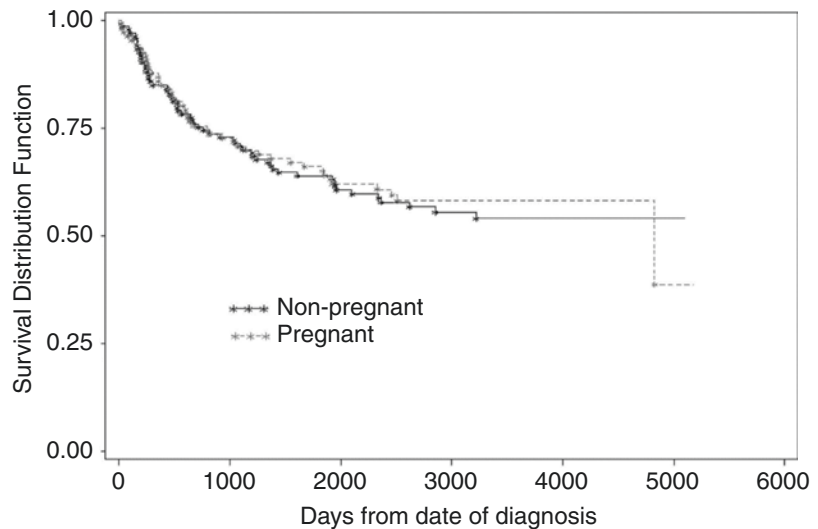
### 18.6.8.1 Maternal Outcome

Around 1900, it was stated that permanent hyperemia, the severe relaxation of the tissues, favors a rapid spread of the process to a very great extent. So, an intense aggravation occurs as a rule far more quickly than in the absence of pregnancy. Some claim that this may be attributed to (1) masking of symptoms related to tumor development as a result of gestation; (2) proliferation and decreased apoptosis of tumor cells due to the effects of various cytokines and hormonal and environmental stimuli related to the state of pregnancy; and (3) the possible state of tolerance to tumor cells acquired in pregnancy as shown to occur in the paternal alloantigens [284].

The prognosis in CRC is largely based on the stage at diagnosis. Pregnant women with CRC are diagnosed at a more advanced stage [228], secondary to delay in diagnosis, leading to a worse prognosis [285]. It is hypothesized that the

development of CRC during pregnancy can be attributed to alterations of the p53 tumor suppressor gene or gene product on the one hand and a maternal immune-tolerant state on the other [286]. In a review of 42 patients with CRC above the peritoneal reflection, 56% of patients died when the cases were reported. Most died within 1 year of being diagnosed, and the median survival for the group was <5 months [287]. One of the possible explanations is a higher percentage of primary signet-ring cell carcinoma, a rare variant of CRC. The incidence is 0.1–0.9% [288]. Microsatellite instability is present in approximately 30% of tumors [57]. This variant of CRC is usually diagnosed at an advanced stage, at a younger age, more likely with lymph node metastasis, an aggressive clinical course, and a poor prognosis [251]. The stage at initial diagnosis in women with pregnancy-associated CRC is no different from the aged-matched, nonpregnant population of women with CRC, with a similar distribution of histological subtypes [220, 228, 285]. This is partly due to the similar histologic subtypes between the two populations of women [219] despite some claiming that pregnant women have higher rates of an aggressive, mucinous subtype [285]. Ultimately, survival was no different among women with pregnancy-associated CRC and nonpregnant women with CRC (Fig. 18.42). No data are available for

**Fig. 18.42** Kaplan–Meier survival distribution for pregnant and nonpregnant women with colon cancer (aged-matched, with a similar distribution of histological subtypes) in California, USA, 1991–1999. (Reproduced with permission from [219])





obstruction CRC in pregnancy because it is an extremely rare condition. CRC during pregnancy presents in a distal distribution (64–86% were in the rectum) and presents at an advanced stage (60% were in the Dukes C stage or more advanced at the time of diagnosis).

Although differences exist between the biology and clinical behavior of anal and colon cancers, all were analyzed together. After the omission of patients with anal cancer, a separate analysis yielded perinatal and cancer outcomes virtually identical to the entire group [219].

Survival in the general population, with metastasis involvement of the ovaries, is poor, ranging from 3 to 12 months [246]. Oophorectomy prolongs survival in patients with ovarian metastases by 10 months [289]. No data exist for the pregnant population. Some recommend prophylactic bilateral salpingo-oophorectomy simultaneous with CRC surgery [290, 291]. In contrast, others did not find the incidence of synchronous and metachronous ovarian tumors to be high, and overall long-term survival was unaffected [253, 292]. However, it is prudent to consider the patient's desire for future pregnancies. Also, bilateral salpingo-oophorectomy at the time of resection has been linked to an increased incidence of spontaneous abortion, especially if performed during the first trimester [246]. Another option is obtaining bilateral wedge biopsies of the ovaries during surgery for the pathologic examination of the frozen sections with subsequent removal if the ovaries are involved [246].

Obstetrical outcomes were good overall, though pregnancy-associated cases of CRC did have higher CS and preterm delivery rates. Pregnant women with CRC had a larger number of major puerperal infections. It is possible that women with CRC are more prone to infections that may be subclinical before delivery but predispose them to preterm labor. This could be secondary to malignancy-related immune suppression or other unknown causes [219]. Another explanation is that CRC initiates an inflammatory reaction that starts the preterm labor cascade secondary to the proximity to the uterus.

### Genetic Counseling

CRC rarely occurs in young patients, so this patient population is more likely to have strong predisposing factors than the general population of patients with CRC [293]. Such predisposing factors for CRC include hereditary nonpolyposis CRC (Lynch syndrome), familial adenomatous polyposis, Gardner's syndrome, Peutz-Jeghers syndrome, and long-standing inflammatory bowel disease. However, these increased risk groups represent only a small portion of CRC diagnosed in pregnancy [226]. A review of 19 pregnant patients by Girard et al. in 1981 demonstrated that 21% had one of these strong predisposing factors for CRC [221]. Despite the negative result for possible hereditary nonpolyposis CRC (*Amsterdam II criteria*), *Bethesda criteria* should be checked for microsatellite instability. If the microsatellite instability testing is positive, the genetic testing of the three genes associated with HNPCC should proceed. Once a mutation was identified in the family, other family members could consider predictive testing.

#### 18.6.8.2 Fetal Outcome

There are no reports of adverse fetal outcomes due to CRC, even with metastatic disease [294]. Despite the higher rates of preterm delivery, neonatal outcomes are excellent [217, 219, 239, 285]. The infant survival rate in pregnancies complicated with CRC is 78.1% [295]. Metastasis to the placenta was reported [296].

Although a complete evaluation of the placenta is recommended, there is no evidence to support periodic follow-up of the baby. Metastasis of CRC to the products of conception has not been described [238].

## 18.7 Intestinal Stomal Obstruction

Stoma-related problems occur in half of the patients [297], 68% during the second and third trimesters. However, these problems are cor-

rected without medical intervention [298]. For example, the enlarging uterus may drag on the ileostomy loop from within, causing stomal retraction. In one study, 10% of patients with ileostomies had an intestinal obstruction during pregnancy [24].

Various causes of local intestinal stomal obstruction occur in the general population, with additional factors in pregnancy (Table 18.7). These causes are extremely rare in pregnant patients due to the rarity of stomas in this population and because most of these stomas are temporary. If the patient had a stoma before pregnancy, during pregnancy, a normal functional stoma could enlarge by at least 20 mm (double) than before pregnancy. This is common and not a sign of ileostomy obstruction or an (incarcerated) parastomal hernia. With a functional stoma, the asymptomatic patient should be reassured, and a diagnostic workup is unnecessary.

Rare patients have intestinal stomas during pregnancy, primarily due to inflammatory bowel disease (Table 18.8). These data refer to the presence of ostomy during pregnancy, not the creation of a stoma.

**Table 18.8** Primary diagnosis for ostomy creation

| Disease               | Percent |
|-----------------------|---------|
| Ulcerative colitis    | 63.6    |
| Crohn’s disease       | 15.2    |
| Malignancy            | 4.6     |
| Bowel injury          | 1.5     |
| Rectovaginal fistula  | 1.5     |
| Small urinary bladder | 1.5     |
| Polyposis coli        | 1.5     |
| Unspecified           | 10.6    |

Reproduced with permission from [297]

**Table 18.7** Causes of intestinal stomal obstruction in pregnancy

|                                    |
|------------------------------------|
| Stomal prolapse                    |
| Stomal intussusception             |
| Stomal stenosis                    |
| Surrounding tumor progression      |
| Parastomal hernia                  |
| Adjacent adhesions and kinking     |
| Compression from the gravid uterus |

**18.7.1 Intussusception and Prolapse**

**18.7.1.1 Incidence**

Intussusception in stoma is extremely rare. Since 1950, more than half (57%) presented during pregnancy [299–301] along with one colostomy intussusception [302].

**18.7.1.2 Risk Factors**

Pregnancy is a risk factor for stomal intussusception because more than 50% of all ileostomy intussusceptions are during pregnancy. There are too few cases for analysis, but in most cases, ulcerative colitis was the underlying disease [299–301]. Whether ulcerative colitis is the cause or most patients with inflammatory bowel diseases have the ileostomy in their reproductive years is unresolved. In the general population, factors increasing intra-abdominal pressure are risk factors for stomal prolapse. Active inflammatory bowel disease causes mucosal edema, which can promote intussusception and a stomal prolapse. Corticosteroid therapy can also promote intussusception/prolapse due to wound healing/fibrous tissue processes. In most cases, an ileostomy was the location of intussusception, which was done before pregnancy [299–301].

**18.7.1.3 Clinical Presentation**

The clinical presentation of intestinal obstruction is the same as any other cause (see Sect. 18.1). Clinical diagnosis is somewhat easier because most patients seek medical attention when the stoma prolapses, commonly before other symptoms develop. Stomal prolapse is rarely accompanied by a stomal obstruction (incarceration) or strangulation. The clinical presentation of stomal intussusception is clinically identical.

**18.7.1.4 Diagnosis**

A patient with a stoma should be evaluated for possible local obstruction. Stomal intussusception is easily confused with stomal prolapse [301], easily reducible, and rarely accompanied by stomal obstruction. If the obstruction is at the

level of a stoma and MRI is not available, ionizing diagnostic modalities are not needed.

### 18.7.1.5 Treatment

#### Intussusception

In all cases during pregnancy, stomal intussusception was treated surgically. Surgical management was different in all three cases: (1) by revision of ileostomy [299], (2) by resection and refashioning of the colostomy [301], and (3) reduction by gentle traction at laparotomy, the lateral space to the stoma was closed, and the ileum attached to the anterior abdominal wall with absorbable sutures [300].

#### Prolapse

In the general population, stomal prolapse is treated conservatively if asymptomatic and without complications such as obstruction, necrosis, or strangulation. Prolapse can be reduced manually or with sugar applied to the prolapsed segment [303]. Even incarcerated prolapse can be successfully treated with these measures [304]. These simple methods avoid operation and anesthesia and can sometimes postpone definitive treatment after delivery. Immediate surgery is mandatory if irreducible prolapse becomes ulcerated, strangulated, or causes intestinal obstruction.

Increased abdominal pressure may occasionally cause an ileostomy prolapse. This usually occurs in patients with an ileostomy placed less than a year before becoming pregnant. This should be taken with caution because temporary ileostomies are closed within 3–6 months.

### 18.7.1.6 Prognosis

After operative treatment of intussusception, maternal survival is 100% [299–302]. In the only case [300], twins survived and were healthy after emergent CS in the 35th week for fetal distress.

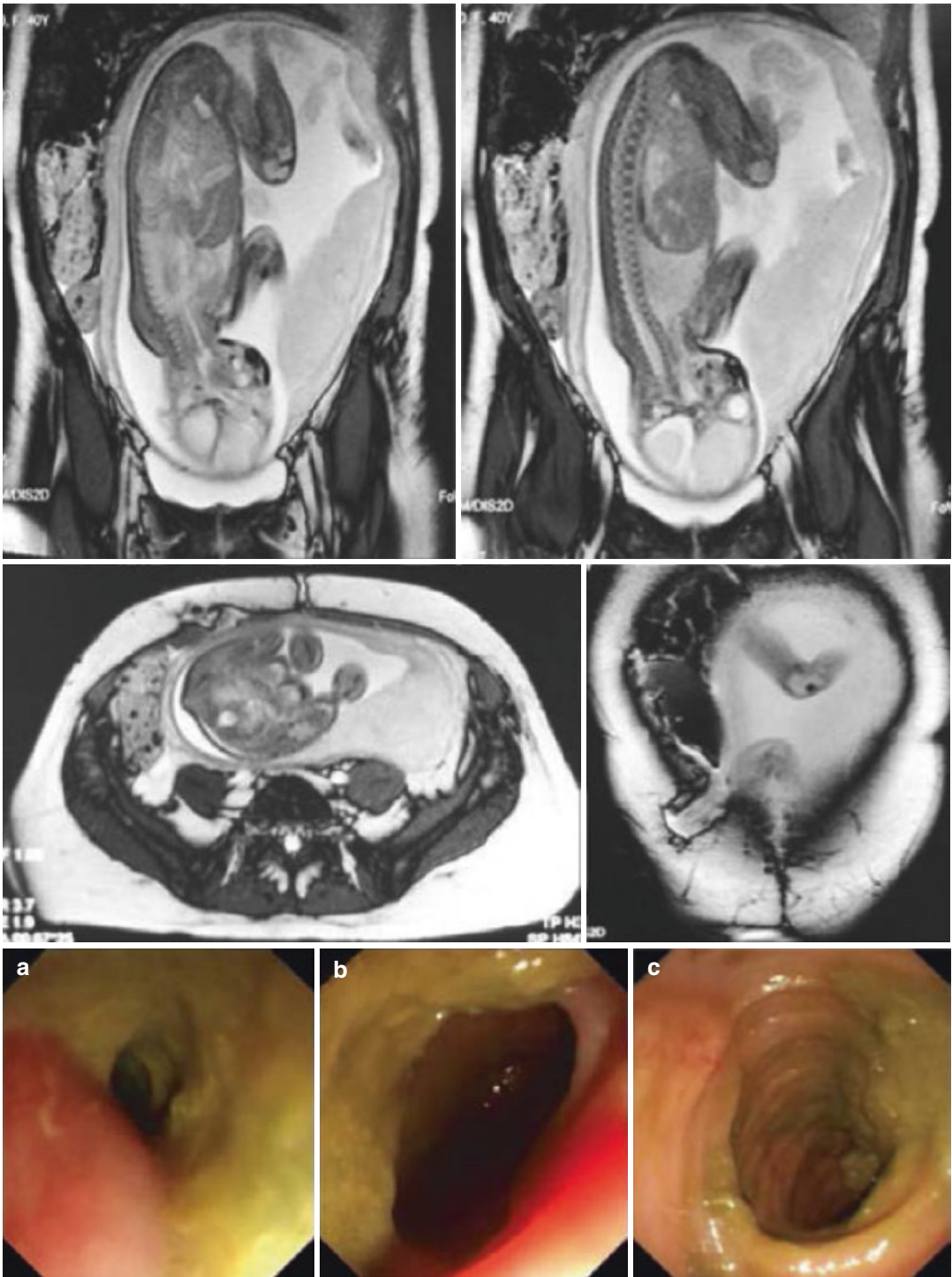
## 18.7.2 Extraluminal Stomal Compression

### 18.7.2.1 Incidence

Condition is extremely rare, with only several cases published [305, 306]. Recent case reports suggest that ileostomy obstruction caused by the enlarging gravid uterus rather than adhesions may be more common than previously recognized [307].

### 18.7.2.2 Diagnosis

Plain abdominal X-rays lack sensitivity and specificity in the gravid patient. Also, it is more difficult to locate the level of intestinal obstruction in pregnant patients. Abdominal MRI can delineate the obstruction site, sometimes with the help of endoscopy (Fig. 18.43). Since 2007, two cases have been published in which MRI was used to correctly diagnose and differentiate ileostomy obstruction caused by compression by the gravid uterus [305, 306]. In both cases, surgical intervention was avoided, and there was a return to normal stomal function immediately postpartum. The adhesions, assumed to be the major cause of bowel obstruction in pregnancy, are not visible on MRI. Their presence is inferred from the absence of obstructing lesions such as a gravid uterus [306].



**Fig. 18.43** Abdominal MRI shows fecalization and distension of the distal ileum terminating just proximal to the end ileostomy at a site compressed by the adjacent gravid uterus and fetus. Below the MRI are photographs showing the endoscopic view through the stoma of the distal ileum,

demonstrating (a, b) extrinsic compression with a thickened, inspissated ileal content, and c) normal distal ileal mucosa proximally. (Reproduced with permission from [305])

### 18.7.2.3 Treatment and Prognosis

Gestational intestinal obstruction has previously been associated with significant maternal and fetal mortality and morbidity. So, the prevailing consensus in the (limited) literature strongly favored aggressive management by urgent surgical intervention in all cases of stomal obstruction [24, 302, 308].

It is important to distinguish between adhesive ileostomy obstructions and mechanical compression on the stoma since treatment for the latter is conservative rather than surgical [306]. Stenting and drainage of the blocked ileostomy by tube or variant have been used without complications [305, 309]. A wide-bore drainage tube can be used to bridge the compressed portion of the bowel [310] or an endotracheal tube to unblock the distorted nipple valve of a Kock's pouch that became obstructed by the enlarging uterus [309]. Other nonsurgical techniques reported to be successful include ileal lavage, massage, hot water bottles, and an elemental diet [298, 299, 310].

## 18.8 Sigmoid Volvulus

### 18.8.1 Incidence

Sigmoid volvulus is the most common cause of large bowel obstruction complicating pregnancy, accounting for 3.1–12.5% [311, 312], up to 25–44% [56]. In endemic regions for Chagas disease in South America, digestive manifestations are common and sigmoid volvulus is possible [313]. Sigmoid volvulus in pregnancy accounted for 2% of all sigmoid volvulus in the Mayo Clinic between 1960 and 1980 [312].

Karl von Rokitsansky, in 1837, described the first case of sigmoid volvulus in the general population [314]. Braun, in 1885, made the first report of term pregnancy with the diagnosis made at autopsy [315]. Six years later, Cattell described the first case in the USA. Lambert [316] reported 29 cases of sigmoid volvulus before 1931, followed by another 12 cases by Kohn et al. [317] between 1931 and 1944. More than 100 cases of sigmoid volvulus have been reported in the pregnancy and puerperium (Table 18.9).

**Table 18.9** Reported cases of sigmoid volvulus in pregnancy

| Authors                 | Year        | Cases | Gestational age (weeks) | Duration of symptoms (h) | Outcome |       |
|-------------------------|-------------|-------|-------------------------|--------------------------|---------|-------|
|                         |             |       |                         |                          | Mother  | Fetus |
| Lambert [316]           | Before 1931 | 29    | –                       | –                        | –       | –     |
| Kohn et al. [317]       | 1931–1944   | 12    | –                       | –                        | –       | –     |
| Harer and Harer [47]    | 1944–1958   | 11    | –                       | –                        | –       | –     |
| Lazaro et al. [318]     | 1958–1969   | 13    | –                       | –                        | –       | –     |
| Fraser and Eckert [319] | 1983        | 1     | 32                      | 24                       | Healthy | Alive |
| Ballantyne [312]        | 1985        | 1     | 3rd trimester           | –                        | –       | –     |
| Hofmeyr [320]           | 1985        | 2     | 33                      | 72                       | Healthy | IUD   |
|                         |             |       | 26                      | 72                       | Expired | IUD   |
| Keating [321]           | 1985        | 1     | 34                      | 24                       | Healthy | Alive |
| Allen JC                | 1990        | 1     | 28                      | 24                       | Healthy | Alive |
| Lord SA                 | 1996        | 1     | 36                      | 24                       | Healthy | Alive |
| Joshi MA                | 1999        | 1     | 28                      | 24                       | Healthy | IUD   |
| De [322]                | 2005        | 1     | 24                      | 72                       | Healthy | IUD   |
| Alshawi [211]           | 2005        | 1     | 28, 35                  | 24                       | Healthy | Alive |
| Iwamoto [323]           | 2007        | 1     | 35                      | 72                       | Expired | IUD   |
| Vo [324]                | 2008        | 1     | 28                      | 24                       | Healthy | Alive |
| Narjis Y                | 2008        | 1     | 24                      | –                        | Healthy | Alive |
| Atamanalp [335]         | 2008        | 9     | 3rd trimester           | 24                       | Healthy | –     |
|                         |             |       | 2nd trimester           | 36                       | Healthy | –     |
|                         |             |       | 3rd trimester           | 72                       | Expired | –     |
|                         |             |       | 3rd trimester           | 20                       | Healthy | –     |

(continued)



**Table 18.9** (continued)

| Authors             | Year | Cases | Gestational age (weeks) | Duration of symptoms (h) | Outcome |       |
|---------------------|------|-------|-------------------------|--------------------------|---------|-------|
|                     |      |       |                         |                          | Mother  | Fetus |
|                     |      |       | 3rd trimester           | 24                       | Healthy | –     |
|                     |      |       | 2nd trimester           | 36                       | Healthy | –     |
|                     |      |       | 3rd trimester           | 12                       | Healthy | –     |
|                     |      |       | 1st trimester           | 22                       | Healthy | –     |
|                     |      |       | 3rd trimester           | 18                       | Healthy | –     |
| Chourak [325]       | 2009 | 1     | 37                      | 48                       | Healthy | IUD   |
| Kolusari [326]      | 2009 | 3     | 7                       | 24                       | Healthy | Alive |
|                     |      |       | 31                      | 48                       | Healthy | IUD   |
|                     |      |       | 32                      | 48                       | Healthy | Alive |
| Machado [327]       | 2009 | 1     | 18                      | 18                       | Expired | Alive |
| Togo [328]          | 2011 | 1     | 25                      | 48                       | Healthy | Alive |
| Khan [329]          | 2012 | 1     | 30                      | 144                      | Expired | IUD   |
| Dray [330]          | 2012 | 1     | 37                      | 12                       | Expired | Alive |
| Nascimento [331]    | 2012 | 1     | 33                      | 72                       | Expired | IUD   |
| Aftab [332]         | 2014 | 1     | 32                      | 48                       | Healthy | Alive |
| Palmucci [333]      | 2014 | 1     | 31                      | 72 + 48                  | Healthy | Alive |
| Kessler [334]       | 2014 | 2     | 30                      | 24                       | Healthy | Died  |
|                     |      |       | 38                      | 120                      | Healthy | Alive |
| Atamanalp [335]     | 2015 | 1     | 16                      | 48                       | Healthy | –     |
| Saxena [336]        | 2015 | 1     | 32                      | –                        | Healthy | Alive |
| Al Maksoud [337]    | 2015 | 1     | 26                      | 120                      | Healthy | Alive |
| Serafeimidis [338]  | 2016 | 1     | 30                      | 48                       | Healthy | Alive |
| Ramalingam [339]    | 2016 | 1     | 34                      | 72                       | Healthy | Alive |
| Ward [340]          | 2017 | 1     | Labor/puerperium        | 24 ?                     | Healthy | Alive |
| Bajaj [341]         | 2017 | 1     | 36                      | 72                       | Healthy | Alive |
| Alrahmani [342]     | 2018 | 1     | 32                      | 24                       | Healthy | Alive |
| Tesnière [343]      | 2018 | 1     | 34                      | 120                      | Healthy | Alive |
| Rottenstreich [344] | 2019 | 1     | 36                      | 120                      | Healthy | Alive |
| Bong [345]          | 2019 | 1     | 32                      | 72                       | Healthy | Alive |
| Cortez [346]        | 2020 | 1     | 30/32                   | 24                       | Healthy | Alive |

IUD, intrauterine death

### 18.8.2 Pathophysiology and Risk Factors

Pregnancy itself is the precipitating factor for sigmoid volvulus. Braun, in 1885, claimed that the pressure of the gravid uterus upon the sigmoid flexure produced constipation, which preceded the attack, and gave rise to elongation of the mesentery and bowel above the seat of compression to a sufficient extent to cause volvulus [315], the hypothesis confirmed by others [47, 337]. The colon rises out of the pelvis and twists around the fixation point on the sigmoid colon and mesocolon. This mechanism may lead to mechanical obstruction and vascular compromise of the bowel [312]. This could explain the increased sigmoid

volvulus incidence during the third trimester [7, 332]. Most cases of the sigmoid volvulus develop during the third trimester (Table 18.9). Sigmoid volvulus in pregnancy mainly affects chronically constipated patients with a long redundant sigmoid colon, as in the general population [312]. High-fiber diets are also a predisposing factor [311], probably due to voluminous, heavy fecal mass prone to position changes due to inertia.

### 18.8.3 Clinical Presentation

The diagnosis of sigmoid volvulus should be suspected when a pregnant female presents with a clinical trial of abdominal pain, distention, and

constipation. The pain can be intense from the beginning or, gradually increasing in intensity, colicky. Initially, it is not associated with vomiting, fever, or anal bleeding [332]. New-onset vomiting progresses to fecal vomiting. The patient may present with fever, dehydration, and absence of bowel sounds. The average time from the onset to hospital presentation is 24–72 h, but even 6 days have been reported (Table 18.9). Largely, this is because pregnancy itself masks the clinical picture since abdominal pain, nausea, and leukocytosis can occur in an otherwise normal course of pregnancy [321].

Recurrent sigmoid volvulus during the same or subsequent pregnancies occurs in 5% [342, 346] after nonoperative treatment. The time to recurrence of volvulus is variable. The duration of symptoms is shorter because patients with previous episodes seek medical help earlier [342, 346].

#### 18.8.4 Differential Diagnosis

The most similar clinical and radiological presentations include cecal volvulus and acute colonic pseudo-obstruction (sy. Ogilvie), most commonly after CS and rarely after vaginal delivery. Before modern imaging, misleading differ-

ential diagnoses resulted in treatment delays for several days [347].

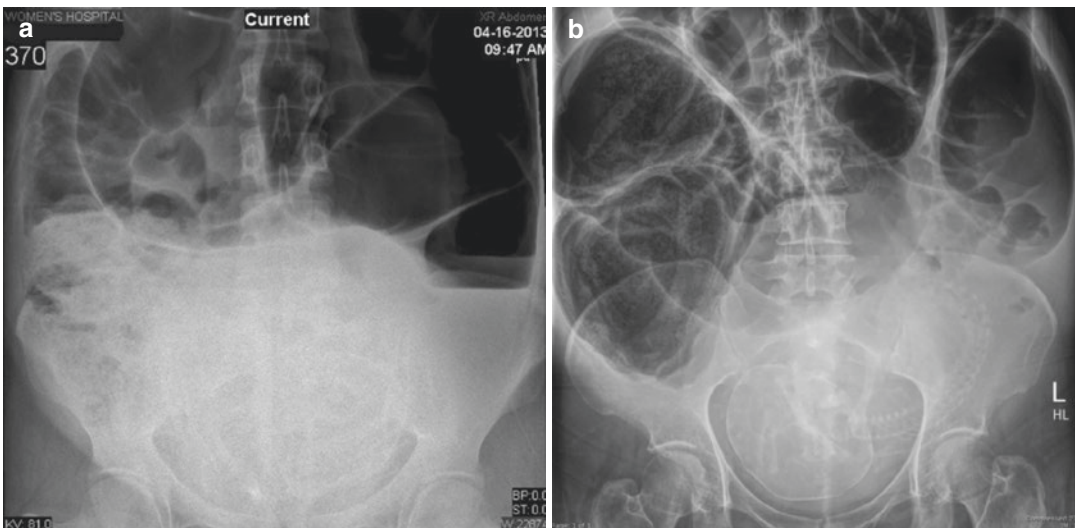
### 18.8.5 Diagnosis

#### 18.8.5.1 Laboratory Findings

Laboratory findings are not specific and normal in the early phase. Leukocytosis can be a consistent sign, but initially, the levels can be normal or slightly elevated [211]. Furthermore, the WBC count is typically elevated in pregnancy. When metabolic derangements due to bowel necrosis and sepsis develop, abnormal laboratory findings are a rule.

#### 18.8.5.2 Plain Abdominal X-Ray

A plain abdominal X-ray is necessary to diagnose intestinal obstruction or volvulus and is sufficient for a definitive diagnosis in early pregnancy. In the 3rd trimester, the enlarged uterus distorts the anatomy, and the diagnosis is challenging (Fig. 18.44) *Coffee bean sign* can be slightly distorted due to the enlarged uterus. *Frimann–Dahl’s sign*: Three linear shadows converging to the left side—a radiographic sign of sigmoid volvulus, are difficult to find in pregnancy due to the distorted anatomy.



**Fig. 18.44** Plain abdominal radiographs of sigmoid volvulus in pregnancy. The characteristics of the sigmoid volvulus (*coffee bean sign*) are distorted due to the enlarged uterus and rectum devoid of gas. (a) At 32 weeks of gestation.

(Reproduced with permission from [332] under the CC BY 2.0) and (b) at 32 weeks of gestation, nonspecific distended large bowel loops with the absence of gas in the rectum. The fetus is visible. (Reproduced with permission from [345])

### 18.8.5.3 Abdominal MRI

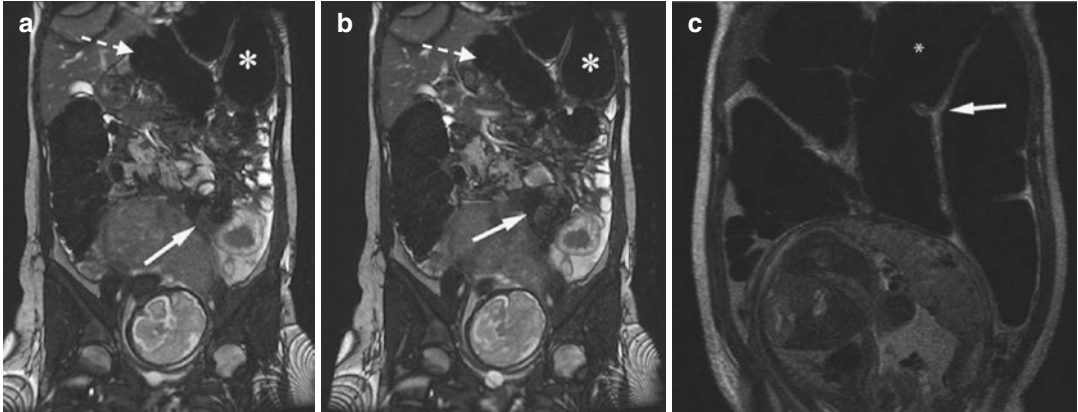
Abdominal MRI has high sensitivity and specificity for diagnosing sigmoid volvulus. Pathognomonic imaging findings are the *coffee bean sign*, the *U-shaped distended sigmoid loops*, the *northern exposure sign*, and the twisting of the sigmoid loop (Fig. 18.45).

### 18.8.5.4 Abdominal CT

If MRI is unavailable, CT shows the same characteristics (Fig. 18.46).

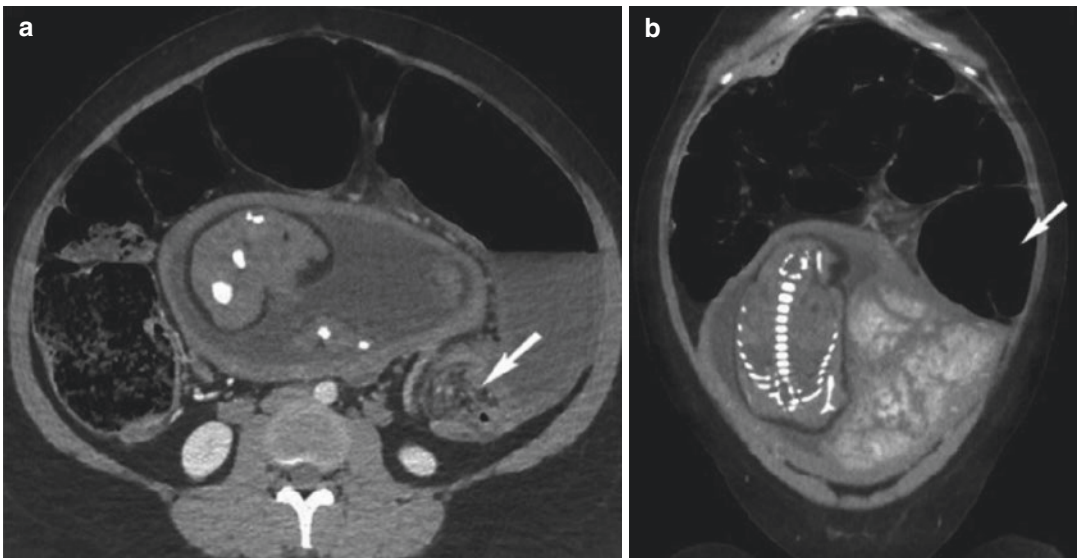
### 18.8.5.5 Colonoscopy

MRI and colonoscopy should be used instead of X-ray studies [348]. A colonoscopic finding of a



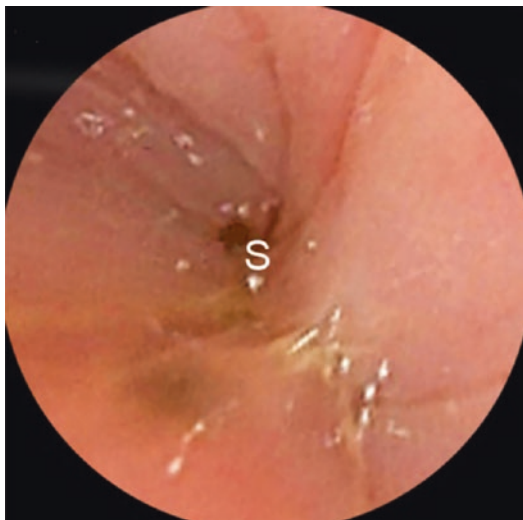
**Fig. 18.45** Abdominal MRI at 31 weeks of gestation. (a, b) The distended sigmoid loop—with an inverted “U configuration” (white asterisks)—extended cephalad to the transverse colon (white dotted arrows) up to the left hemidiaphragm. The displacement of the sigmoid colon cephalad to the transverse colon produces the *northern exposure sign*. The figures also show the partial twisting of the sigmoid loop (white arrows), resulting in dilation and obstruction. (c) *Coffee bean sign* recognizable between

two closed and dilated apposed loops, recalling the appearance of a “coffee bean.” The central cleft of the coffee bean is due to the opposing bowel wall (white arrow). The *U-shaped distended sigmoid loop* is also well depicted: a distended ahastral sigmoid loop (white asterisk), with an inverted “U configuration,” extended up to the left hemidiaphragm; the transverse colon is dilated and displaced to the right side by the U-loop. (Reproduced with permission from [333] under the CC BY 2.5)



**Fig. 18.46** (a) Axial CT of the abdomen shows bowel obstruction with a transition point at the level of the sigmoid colon and “whirl sign” (arrow). (b) Coronal abdom-

inal CT image shows sigmoid colon dilation (arrow) and rectum devoid of gas. (Reproduced with permission from [343])



**Fig. 18.47** Endoscopic appearance of sigmoid volvulus in a pregnant woman. *S* spiral sphincter-like twisted sigmoid lumen. (Reproduced with permission from [348])

pregnant patient with sigmoid volvulus is not different from that of a nonpregnant patient. It includes a spiral sphincter-like twist of the lumen (Fig. 18.47).

## 18.8.6 Treatment

### 18.8.6.1 Conservative Treatment

In the first trimester, a nonoperative procedure using colonoscopic detorsion and rectal tube decompression is recommended until the second trimester, when sigmoid colectomy is performed for recurrent cases [211]. Also, mucosal ischemic changes can be detected by colonoscopy. Vital mucosa indicates endoscopic decompression. If signs of mucosal ischemia are found, emergent laparotomy with sigmoid resection is mandatory [335]. The same principles apply to the third trimester [211]. Colonoscopic decompression and detorsion success rate is 83% [349].

Endoscopic treatment of recurrent sigmoid volvulus is safe, feasible, and preferred over surgery in pregnant patients who are hemodynamically stable and do not have signs or symptoms of acute perforation or bowel ischemia. This modality can be used multiple times for recurrent volvulus until delivery [346].

### 18.8.6.2 Surgical Treatment

The management of volvulus with or without perforation in pregnant and nonpregnant women is similar. Surgical treatment aims to remove the obstruction without risk of recurrence. The basis of therapy is early surgical intervention. In the absence of peritonitis and during the second trimester of gestation in the 1950s, some recommended detorsion by minilaparotomy [322]. Such an approach shortens the operating time, whereas sigmoid resection with anastomosis is performed after puerperium [350]. This approach is still used [351, 352].

Sigmoid resection is recommended due to the high incidence of recurrence with other non-resectional interventions [210, 211, 341]. Others recommended anastomosis after sigmoidectomy during the first and second trimesters [353]. Hartmann's procedure is mandatory with gangrenous bowel. It eliminates the risk of anastomotic dehiscence, which can result in abortion, death in utero, preterm labor, and maternal complications [322, 354]. The growing uterus could compress the anastomosis, causing ischemia (Fig. 18.48), or compress the colon distal to the anastomosis, increasing the risk of anastomotic dehiscence. A CS must be carried out in the third trimester if sufficient intestinal exposure cannot be obtained due to the enlarged uterus [355]. After detorsion, the deflated loop could be on the left side of the abdo-





**Fig. 18.48** Dilated ischemic sigmoid colon from volvulus compressed by the gravid uterus. (Reproduced with permission from [337] under the CC Attribution License)

men and should be replaced without even uterine management. This could be done by slipping the bowel loop over the uterine fundus. Uterine compression on the colon contributes to obstruction when the volvulus is partial. The entire bowel should be examined for other areas of obstruction and intestinal viability. If viable, it can be derotated and left in situ [333, 338], but recurrent sigmoid volvulus in the general population is approximately 50%. Therefore, resection during the index operation with or without anastomosis is recommended [355]. Despite the widespread use of laparoscopic colorectal operations, advanced pregnancy precludes colonic resections due to limited visibility and organ manipulation [356].

If CS is indicated preoperatively or the fetus has reached viability, low median laparotomy is the best approach for both CS and colonic operations [351]. CS should be performed before colonic resection to minimize uterine wound contamination, endometritis, or newborn infection and enable more intraoperative manipulative space [351].

### 18.8.7 Prognosis

A delay in diagnosis and surgical intervention significantly impacts the outcome of the mother and fetus [47]. The delay in diagnosis

of sigmoid volvulus may lead to bowel infarction and necrosis [338] with hypovolemia, electrolyte disturbances, renal failure, metabolic acidosis, septic shock, and multiple organ failure. The maternal and fetal outcome has been directly related to the degree of bowel ischemia and subsequent sepsis. Maternal and fetal mortality from 1978 to 2012 was 20% and 40%, respectively [329]. Maternal mortality has been 5% with viable bowel but rises to over 50% with bowel perforation. Recent maternal and fetal survival is 100% (Table 18.9).

Most maternal and fetal deaths occurred with a delay in presentation and intervention of >48 h.

## 18.9 Cecal Volvulus

### 18.9.1 General Considerations

Volvulus of the cecum is torsion of the bowel around its mesentery, resulting in a closed-loop obstruction. Cecal volvulus can occur in 11–25% of the population. It results from proximal colon hypermobility due to inadequate lateral peritoneal fixation during development [12, 190]. Furthermore, the distal ascending colon must be fixed, resulting in a pivot point where the cecal rotation may occur. While these fixation points are typically the normal congenital peritoneal attachments, other possibilities include postoperative adhesions or an abdominal mass. In pregnancy, the enlarged uterus may displace any redundant or abnormally mobile cecum out of the pelvis. Partial obstruction may occur from uterine pressure or from kinking of the colon at a fixed point. The ensuing distension raises the colon even higher, producing torsion at this fixed point [47, 357].



### 18.9.2 Historical Perspective

Rokitansky, in 1841, published the first report of cecal volvulus in the general population. Clifford White, in 1914, described the first case of cecal volvulus in pregnancy. The 26-year-old, in her 33-week second pregnancy, was constipated for 6 years after the drainage of the abscess of appendicular origin with an incisional hernia (presumably midline incision). The patient expelled the stillbirth, and an indication for the operation was made after several days. The cecal and ascending colon gangrene due to volvulus was found. Resection was performed, but the patient died [358]. Charles Donald, in 1927, described a 27-year-old epileptic in the 5th month of pregnancy. She had abdominal pain, absolute constipation, and stercoreal vomiting. Exploration revealed gangrene of the small bowel and the cecum near the spleen. Cecostomy was made due to hemodynamic instability. The death occurred 4 h later [359]. Margaret Basden, in 1934, reported the case of a woman in labor in whom laparotomy with CS was done for a suspected intra-abdominal condition, and volvulus of the cecum was found [360]. Spence in 1937 quoted a case of volvulus shortly after delivery in which too much attention was paid to the associated uterine infection. He stated that *during pregnancy and the puerperium, there should not be much delay in performing laparotomy in doubtful cases* [361]. This recommendation was confirmed in 1941 when a patient presented 17 h after delivering a stillborn by forceps. During an extensive diagnostic workup, the patient died. The autopsy showed cecal volvulus and part of ascending colon were found [362].

### 18.9.3 Incidence and Risk Factors

*In view of the rapid change of position of the intestines after delivery of a full-term child, it is perhaps surprising that volvulus does not happen more frequently.*

(J. H. Spence, 1937)

*As a sine qua non for the development of a twist of the right colon, it must have a long mesentery.*

(John Homans, 1921 [363])

Cecal volvulus occurs in 1/500,000–1/1,000,000 pregnancies [364]. It accounted for 2% of all colonic volvulus in the Mayo Clinic between 1960 and 1980 [312]. In 1944, of 79 reported cases of volvulus in pregnancy, 19 were of the right colon [317]. Until 1949, cecal volvulus represented 10% of all cecal volvulus cases published [365].

In 1944, multiparity was defined as a risk factor. Due to adhesion from the previous operations, the fixed cecum is a predisposing factor [366]. Age does not appear to affect the incidence [317].

### 18.9.4 Clinical Presentation

Bowel obstruction from cecal volvulus is similar to sigmoid volvulus (see Sect. 18.8.3). The symptoms and findings at the clinical examination are often vague and indistinguishable from the usual symptoms attributed to late pregnancy or other causes of an acute abdomen. Vomiting is more common with cecal than sigmoid volvulus. With sigmoid volvulus, the ileocecal valve can be competent (for some period during distal obstruction).

### 18.9.5 Differential Diagnosis

In pregnancy, cecal volvulus may be mistaken for placental abruption, degenerating fibroids, a ruptured uterus, hyperemesis, torsion of the ovary, extrauterine pregnancy, acute polyhydramnios, cholecystitis, appendicitis, urinary tract infections with or without urolithiasis, and other causes of bowel obstruction [367, 368].

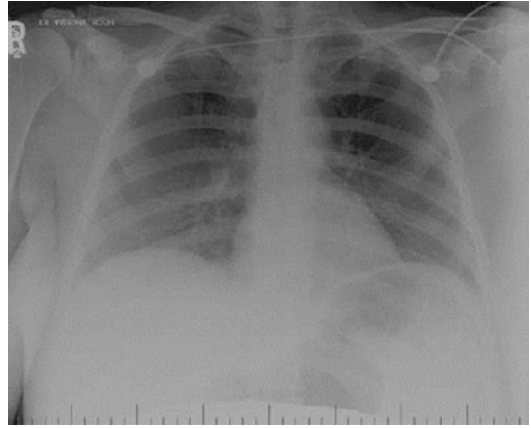
The most similar clinical and radiological presentations include sigmoid volvulus and acute colonic pseudoobstruction (sy. Ogilvie), most commonly after CS but also after vaginal deliv-

ery. Even with preterm vaginal delivery, early postdelivery cecal volvulus is possible [369].

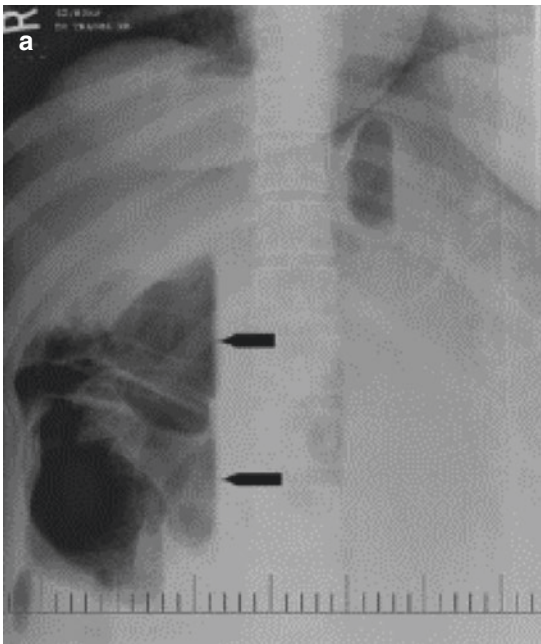
### 18.9.6 Diagnosis

Preoperative diagnosis of cecal volvulus is 25% [47, 357].

Plain abdominal X-ray has a high sensitivity for diagnosing cecal volvulus in pregnancy [370], but sometimes obstruction can only be recognized on plain abdominal radiographs (Figs. 18.49 and 18.50). The diagnosis may be obscured if the closed loop is filled with fluid, oriented in an anteroposterior plane, or overlain by loops of air-distended bowel. The intermittent abdominal pain may be misinter-

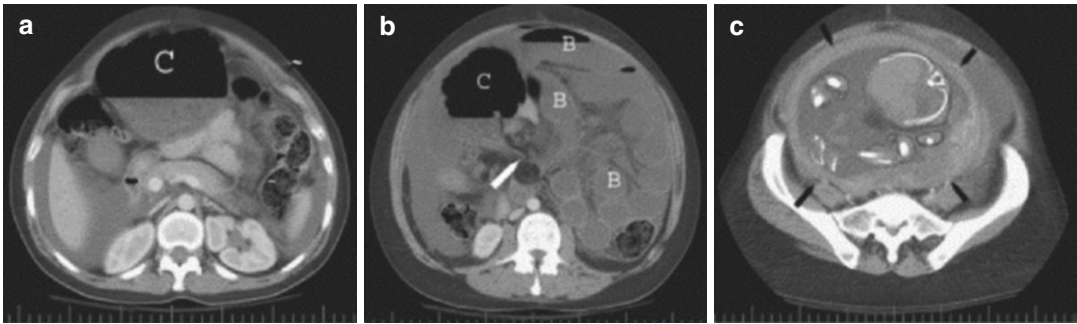


**Fig. 18.49** Erect chest radiograph shows dilated air-filled bowel loops under the left hemidiaphragm with shielding of the lower abdomen. (Reproduced with permission from [366])



**Fig. 18.50** Diagnosis of cecal volvulus is difficult on plain abdominal X-rays, especially in advanced pregnancy. (a) Right lateral decubitus radiograph shows dilated bowel loops with air–fluid levels (*arrows*). (Reproduced with permission from [366]). (b) At

14 weeks of gestation, abdominal supine X-ray shows a dilated bowel loop in the left upper quadrant, with no definable colon to the right of midline and no evidence of free intraperitoneal air. (Reproduced with permission from [370])



**Fig. 18.51** (a) Axial abdominal CT shows a dilated cecum with an air/fece level in the mid-upper abdomen; (b) The dilated cecum (C) shows progressive tapering terminating at the site of torsion (*white arrow*), resulting in the appearance of a *bird's beak*. Dilated fluid-filled loops of the small bowel (B). Compared with the normally

enhancing small bowel loops, the lack of normal mural enhancement of the cecum on CT suggests ischemia. The cecum was necrotic at the surgery. (c) Axial views of the lower abdomen show the gravid uterus (*black arrows*). (Reproduced with permission from [366])

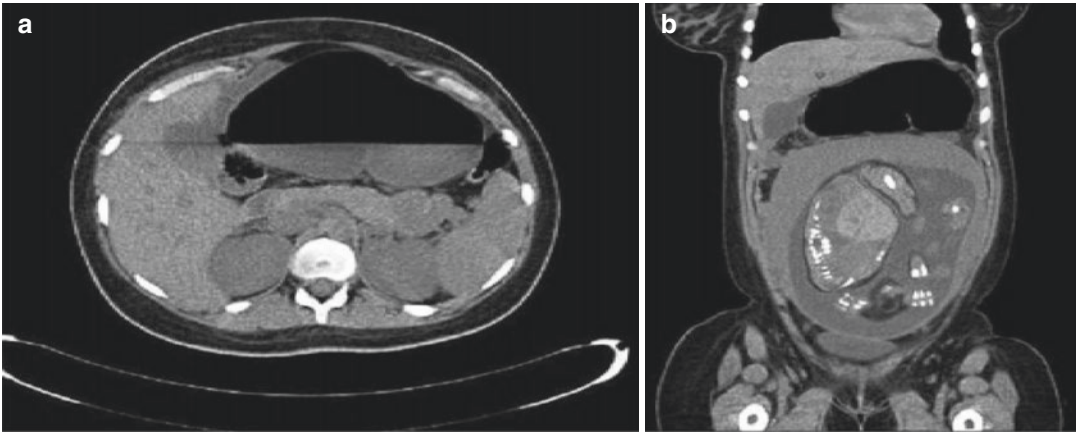
preted as uterine contractions, and emergency CS for intestinal volvulus has been described [357].

When CT is considered appropriate, a senior radiologist should always be involved in decision-making to avoid overutilizing a potentially harmful test. Low-dose CT protocols for imaging the acute abdomen in pregnancy minimize fetal irradiation. CT has high sensitivity and specificity for delineating cecal volvulus in pregnancy (Figs. 18.51 and 18.52). It is difficult to diagnose from a single CT slice, although the cecal volvulus is more “rounded” than the sigmoid volvulus. The *coffee bean sign* helps establish the diagnosis (Fig. 18.53).

MRI is increasingly used in pregnant patients. MRI has been used extensively to characterize and stage neoplastic disease in pregnant women and evaluate the acute abdomen, primarily acute appendicitis in pregnancy (see Chap. 15).



**Fig. 18.52** Abdominal CT in 21 weeks of gestation shows cecal volvulus. The cecum is distended in the right upper quadrant. There is no colonic distension distally, with multiple loops of the distended small bowel. (Reproduced with permission from [372])



**Fig. 18.53** Cecal volvulus can be in both upper quadrants in advanced pregnancy. Complete CT sequence analysis is needed for the diagnosis. The *coffee bean sign* helps in the diagnosis [373]

Abdominal MRI may demonstrate the site of transition in bowel obstruction and identify areas of inflammation, abscess formation, or bleeding within the abdomen and pelvis [371].

### 18.9.7 Treatment

*During pregnancy and the puerperium, there should not be much delay in performing laparotomy in doubtful cases.*

(J. H. Spence, 1937)

In the first half of the twentieth century, surgical options were cecopexy and cecostomy [374]. Current surgical options include open or laparoscopic cecal detorsion [375] with or without appendectomy, colonic detorsion, cecopexy or cecostomy, and right hemicolectomy (mandatory for the necrotic bowel). Laparoscopic procedures, especially hemicolectomy, can be completed during the first trimester. In advanced pregnancy, the lack of visualization and displacement of bowel segments precludes the safe completion of the operation (Fig. 18.54). Laparoscopic cecopexy with appendectomy can be performed in advanced pregnancy or early postpartum [376]. Evidence from the general and pregnant populations suggests that cecal volvulus recurrence (even in the same preg-



**Fig. 18.54** Necrotic cecum at 27 weeks of pregnancy. An enlarged uterus (*lower part*) in advanced pregnancy makes open hemicolectomy (*upper part*) more difficult and precludes laparoscopic resection. (Reproduced with permission from [379])

nancy) due to the hypermobile cecum, with either detorsion, cecopexy, or cecostomy, is unacceptably high [368, 377].

Right hemicolectomy is the treatment of choice for cecal volvulus in pregnancy.



During the 1st and 2nd trimesters or when simultaneous CS is performed, ileotransverse anastomosis is preferred [373, 378]. CS should be performed before colonic resection to minimize uterine wound contamination and endometritis or newborn infection [373]. In continuing 3rd trimester pregnancy, consider ileostomy due to the potential compression of the distal colon by the enlarged and enlarging uterus. Partial distal colonic obstruction can result in anastomotic dehiscence with deleterious effects on the fetus, maternal laparotomy wound, and prolonged maternal abdominal sepsis.

- *Intersigmoid hernia*: Herniation into an intersigmoid fossa at the attachment of the lateral aspect of the sigmoid mesocolon,
- *Transmesosigmoid hernia*: Incarceration of intestinal loops through an isolated, oval defect in the sigmoid mesocolon,
- *Intramesosigmoid hernia*: A congenital, oval defect unrelated to the intersigmoid fossa, present in the lateral peritoneal surface of the mesocolon.

## 18.9.8 Prognosis

### 18.9.8.1 Maternal and Fetal Outcome

Up to 1940, due to the complex clinical picture and limited diagnostic modalities, maternal and fetal mortality was 26.3%. During the last several decades, maternal mortality was nil [380].

## 18.10 Incarcerated Internal Hernia

### 18.10.1 Bariatric Surgery

See Sect. 23.3.

### 18.10.2 Congenital Defects

#### 18.10.2.1 Sigmoid Mesocolon Hernia

##### Incidence

Sigmoid mesocolon hernia is an uncommon type estimated for 6% of internal hernias [381, 382]. Up to 2005, there were 15 cases of transmesosigmoid hernias in the general population (see section “Classification”) [382]. There are only two cases in pregnancy and postpartum published (see section “Etiology”).

##### Classification

Benson and Killen, in 1964, classified these hernias in the general population into three types [383]:

##### Etiology

Pathologic apertures of the mesentery and visceral peritoneum are primarily due to congenital, surgical, traumatic, inflammatory, or circulatory etiologies [381]. Congenital causes of sigmoid mesocolon hernias have also been proposed as possible causes [382]. However, the role of congenital factors remains obscure and theoretical. Some case reports have documented transmesosigmoid hernias developing during pregnancy or postpartum [382, 384]. The authors proposed that dilation and shrinkage of the uterus concomitant with pregnancy or delivery contributed to the development of transmesosigmoid hernias. The abnormal aperture could have been formed from the sigmoid mesocolon tearing by traction due to postpartum shrinkage of the enlarged uterus. One of the theories is that herniation could have occurred a few decades later through the abnormal aperture formed during the pregnancy.

##### Clinical Presentation

The clinical features of an internal hernia are abdominal pain, distention, and vomiting. Most patients complain of left lower abdominal pain.

##### Diagnosis

Plain abdominal X-ray shows distended small bowel loops and air–liquid level formation, suggesting mechanical obstruction.

The key CT findings for the diagnosis of a transmesosigmoid hernia include [385] the following:



- A cluster of dilated fluid-filled loops of the small bowel entrapped in the left posterior and lateral aspect of the sigmoid colon through a mesosigmoid defect,
- The defect is located between the sigmoid colon and the left psoas muscle,
- The sigmoid colon shows anterior and medial displacement,
- Encapsulated loops of the small bowel showed U- or C-shaped configurations and wall thickening, representing closed-loop obstruction and ischemic change,
- Attached mesentery with vessels engorgement and fat obliteration indicating strangulation,
- The proximal small bowel shows dilation.

However, in most cases, the diagnosis of a transmesosigmoid hernia is confirmed by surgical intervention in the general population [386].

Abdominal MRI can precisely define the type and location of an internal hernia (Fig. 18.55). In previously operated patients, finding the cause of obstruction is difficult.

### Treatment

Patients with SBO not responding to conservative management require an operation. If an internal hernia is suspected, the operation should be prompt, as strangulation and gangrene of the bowel are

likely to occur if the surgery is delayed. The role of laparoscopy in patients with intestinal obstruction is increasingly recognized in the general population. However, its role in pregnancy is unclear due to the small number of pregnant patients. The necrosis of the strangulated intestine occurs in up to 80% of patients with a transmesosigmoid hernia, necessitating small intestine resections [388].

### Prognosis

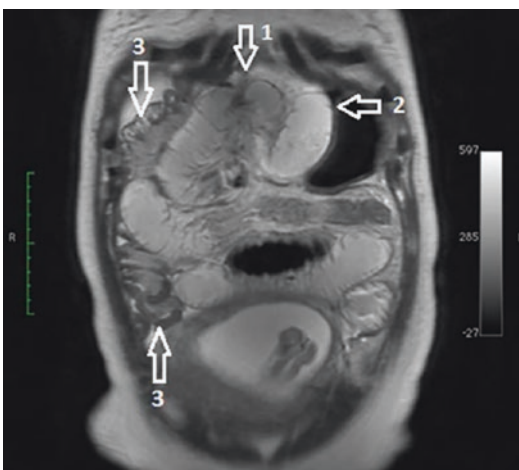
The maternal outcome is excellent because there were no massive bowel resections in both cases, and the pregnant population is mostly young and without comorbidities.

#### 18.10.2.2 Transomental Hernia

Idiopathic transomental herniation in the general population is an extremely rare cause of SBO, accounting for just 1–4% of intra-abdominal herniation cases [389]. There is only one case published during pregnancy with a confusing intraoperative description, different from the one found in the article's title (*there was a hernia sac between the root of the mesentery and transverse mesocolon*). The patient was discharged on the 5th postoperative day with continuing pregnancy. She went into labor at term and had a labor epidural, and emergency CS was due to suboptimal cardiotocography. A healthy female was born [390].

#### 18.10.2.3 Falciform Ligament Hernia

A hernia through the falciform ligament accounts for 0.2% of internal hernias, and most are asymptomatic. Compared to the general population, the incidence could be increased due to a physiologic increase in intra-abdominal pressure, increasing the possibility of an (incarcerated) internal hernia. A congenital cause of these defects is rare, attributable to malformation and incomplete development of the falciform ligament. There are two cases in pregnancy. One case in 20 weeks of pregnancy is published with the classic clinical presentation of SBO. The falciform ligament should be divided by the open or laparoscopic approach. Division prevents future herniations. Both published cases delivered healthy babies by CS [387, 391].



**Fig. 18.55** Abdominal MRI shows elements of herniation: (1) site of herniation; (2) dilated intestinal loop; (3) collapsed intestinal loop. (Reproduced with permission from [387] CC BY 3.0)

## 18.11 Gastric Outlet Obstruction

### 18.11.1 Heterotopic Pancreas

#### 18.11.1.1 Incidence

Heterotopic pancreas (HP) in the general population is often found incidentally in patients operated on for other reasons or during autopsies. The condition is relatively uncommon; it has been found in 0.6–13% of patients in autopsy studies [392, 393] and encountered in 1/500 operations in the upper abdomen [394–396]. A few cases of HP as a cause of gastric outlet obstruction in infants, children, and adults [392, 397, 398] have been published.

One case of gastric outlet obstruction in pregnancy was due to HP [73] and another was due to the active chronic peptic ulcer [399].

#### 18.11.1.2 Embryology

It is possible that early in fetal life, during rotation of the foregut and fusion of the dorsal and ventral parts of the pancreas, small parts are separated from it and continue to develop in the wrong location. Often, HP is found in the stomach, duodenum, and jejunum, but it may also be found anywhere in the digestive tract, intra-abdominally, mediastinum, and lung.

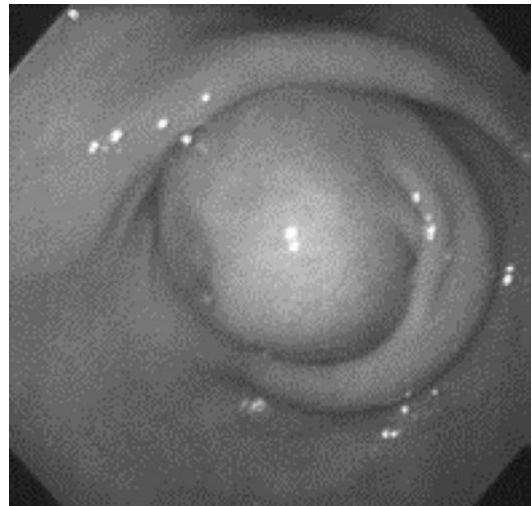
#### 18.11.1.3 Clinical Presentation

The symptoms can be (a) non-emergent, such as epigastric pain (77%) and abdominal fullness (30%), (b) semi-urgent as tarry stools (24%) due to ulceration, or (c) emergent as due to intussusception and obstruction [394, 400]. Gastric outlet obstruction mostly presents first as postprandial vomiting and weight loss with the progression of vomiting [397, 398]. Although HP often exists from childhood, it seldom causes symptoms. Conditions that trigger this previously asymptomatic disorder to become symptomatic include bacterial infection and pancreatitis causing pancreatic edema [401, 402], and there is only one report of an ectopic pancreas becoming symptomatic due to pregnancy [73]. The cause of the symptoms could be

due to the enlarging uterus that narrowed both the gastroduodenal canal and the peritoneal space, although the ectopic pancreas existed beforehand. The relationship between the enlargement of an HP due to the hormonal changes in gestation is unclear.

#### 18.11.1.4 Diagnosis

Preoperative diagnosis is difficult despite modern diagnostic procedures such as the abdominal US, esophagogastroduodenoscopy (Fig. 18.56), and contrast-enhanced abdominal CT [400]. In the general population, preoperative diagnosis of HP was 6% [400]. In the only published case in pregnancy [73], an accurate diagnosis could not be made from the abdominal MRI findings because of the contrast medium restrictions and the motion artifact of the fetus (Fig. 18.57). Degenerated GIST is similar to a submucosal tumor with a central cyst, although it usually grows extraluminally in the upper stomach. In conclusion, HP should be considered in the differential diagnosis of a potentially obstructive gastric submucosal tumor, even though it is rare.



**Fig. 18.56** Preoperative gastroscopy shows a submucosal tumor prolapsing through the pyloric ring and obstructing the gastric outlet. (Reproduced with permission from [73])



**Fig. 18.57** T2-weighted MRI shows a  $4.7 \times 3.6 \times 2.4$  cm target-like tumor in the posterior wall of the gastric antrum (arrowhead). The relatively large central portion shows a high signal intensity suggesting cystic components. The fetus is in the lower abdomen. (Reproduced with permission from [73])

#### 18.11.1.5 Treatment

There are two standard procedures for gastric outlet obstruction. One is endoscopic balloon dilation (especially suitable for peptic gastric outlet obstruction), and another is surgery. Surgery is always indicated when there is a suspicion of malignancy. Full-thickness biopsy of the lesion at surgery is mandatory for establishing the diagnosis of HP from a frozen section; however, this carries the risk of scattering cells if there is a malignant disease [395]. This disorder can be treated by various procedures, including bypass gastroenterostomy or antrectomy with gastroduodenal anastomosis [395, 396]. Lymphadenectomy is not considered necessary as lymphatic spread rarely occurs from an HP or GIST [403]. Less invasive surgery can successfully be performed through a small skin incision. Antrectomy without lymph node dissection was most appropriate to avoid interruption of the pregnancy.

Histologically, HP with mucus retention of the gastric antrum needs to be differentiated from duplication, and although rare, mucinous adenocarcinoma arises from the ectopic gastric pancreas

[404]. Frozen sections at the surgery are not enough to distinguish these three diseases without verifiable pancreatic tissue [405]. Duplication of the stomach can be ruled out if the lining of the cysts does not consist of the normal gastric mucosa.

## 18.12 Gynecologic Causes

A known cause of intestinal obstruction helps in management strategy. Gynecologic causes are described in separate chapters. Gynecologic conditions would unlikely be considered as an underlying cause of intestinal obstruction.

### 18.12.1 Ovarian Teratoma

#### 18.12.1.1 Incidence

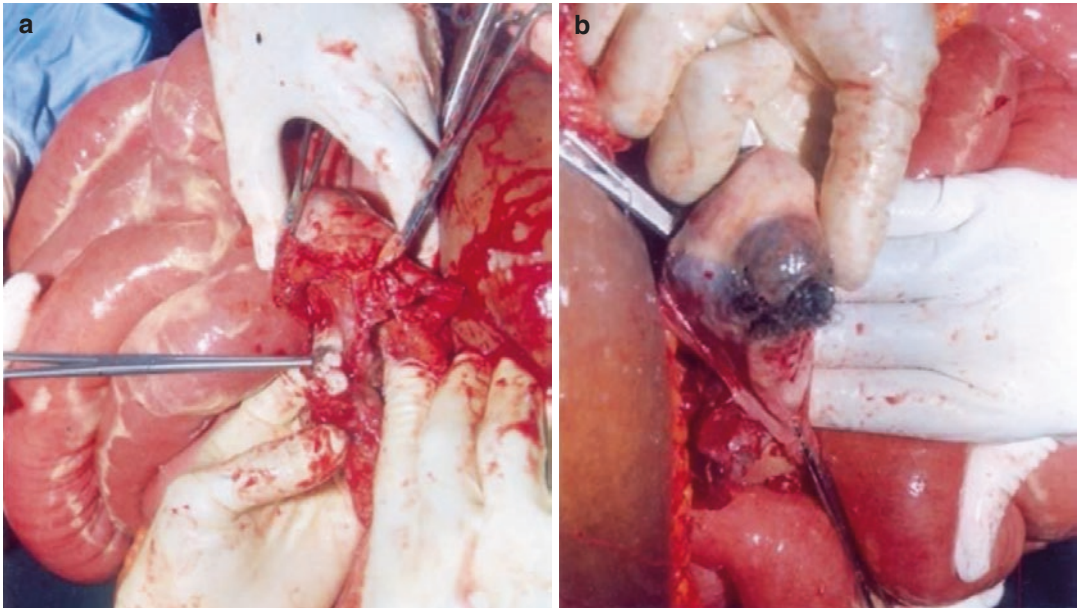
The occurrence of teratoma with pregnancy is uncommon. Approximately 10% of mature cystic teratomas are diagnosed during pregnancy [406], mostly during the second trimester [407, 408]. Mature cystic teratomas usually occur in young women, with a peak incidence between 20 and 40 years [409].

#### 18.12.1.2 Clinical Presentation

The most frequent symptom of teratoma is lower abdominal pain, and only a few cases present for the first time with an abdominal mass. Though the complications of teratoma in pregnancy include torsion, rupture, and obstruction of the birth canal, one case is associated with intestinal obstruction [407]. There was a 2-week history of abdominal pain, abdominal distension, and vomiting. The colicky pain was located in the umbilical region. There was associated constipation with signs of generalized abdominal tenderness.

#### 18.12.1.3 Diagnosis

Concerning diagnosis, an abdominal US (trans-abdominal and transvaginal) scan is the method of choice. In the single case report, a repeat US also reported a singleton intrauterine pregnancy with vague abdominal masses on both sides of the uterus and distended bowel loops. It can determine the dimension of the tumor [407].



**Fig. 18.58** (a) Teeth and other structures of benign ovarian teratoma causing small bowel obstruction with dilated loops; (b) intra-abdominal teratoma being teased from

distended bowel loops. (Reproduced with permission from [407])

#### 18.12.1.4 Treatment

Intestinal obstruction in pregnancy mandates a laparotomy. Findings at surgery were bilateral ovarian masses (benign cystic teratoma) with the right causing kinking of the small intestine (ileum). The right mass adhered partially to the ileum and was separated from it without difficulty (Fig. 18.58). The adhesion might have resulted from a response of the surrounding tissue, including the intestine, to the pressure effect of the tumor. On the other hand, it might have also resulted from a minor leak of tumor content into the surrounding tissue. However, there was no evidence of invasion of the intestinal wall, thus ruling out gross features of malignancy. The size of both tumors was approximately 15 cm in diameter. This tumor possibly existed before the onset of pregnancy.

The teratomas <6 cm occurring before pregnancy do not grow during pregnancy [410].

#### 18.12.1.5 Prognosis

As the tumor was benign, the pregnancy was carried to term, and she delivered a male baby by spontaneous vertex delivery with an APGAR score of 7 at 1 min and 8 at 5 min [407].

### 18.12.2 Ectopic Pregnancy

#### 18.12.2.1 Incidence

Most complications of ectopic pregnancy are in the form of tubal rupture with massive bleeding and hemorrhagic shock. Less than 10 cases of intestinal obstruction due to ectopic pregnancy have been published. In most cases, obstruction was at the level of the terminal ileum [411–415]. One ectopic pregnancy had an additional mass effect, with the myomatous uterus compressing the sigmoid colon [416].

#### 18.12.2.2 Clinical Presentation

Rarely intestinal obstruction and ectopic pregnancy can present simultaneously. The most common signs and symptoms of ectopic pregnancy include amenorrhea, abdominal pain,



irregular vaginal bleeding, and pain on abdominal or pelvic examination. A pelvic adnexal mass is palpated in only 50% of the patients. Unfortunately, the most common signs and symptoms of ectopic pregnancy are correct in predicting only 50% of cases [417]. Abdominal pain is the single most consistent feature of ectopic pregnancy [418] but can be masked due to other symptoms of intestinal obstruction. Clinicians should have a high index of suspicion for ectopic pregnancy in patients with a previous history of tubal pregnancy, tubal surgery, pelvic inflammatory disease (PID), tubal disease, endometriosis, the abdominal surgery itself, intrauterine device, fertility treatment, smoking, and history of multiple sexual partners. The presentation of bowel obstruction is described earlier in the chapter (see Sect. 7.1).

#### 18.12.2.3 Differential Diagnosis

Differential diagnosis of intestinal obstruction due to ectopic pregnancy includes all possible causes of intestinal obstruction. A common confusion is growing uterine fibroid in pregnancy (see Chap. 12), causing bowel compression.

#### 18.12.2.4 Diagnosis

Increased chances of correct diagnosis of an ectopic pregnancy are possible with accurate menstrual and sexual history and availability of serum  $\beta$ HCG measurement and the transvaginal US (see Chap. 15). The transabdominal US is of little help due to dilated bowel loops, which prevent adequate visualization. The diagnosis of bowel obstruction is described earlier in the chapter, and the diagnostic algorithm is standard when an intestinal obstruction is suspected. These diagnostic modalities cannot reveal ectopic pregnancy as the cause of obstruction. A plain abdominal X-ray shows air–liquid levels indicating small or large bowel obstruction [412].

#### 18.12.2.5 Treatment

There are several therapeutic options for ectopic pregnancy *per se*, including medical, expectant, and surgical (see Chap. 15). In cases

with intestinal obstruction due to ectopic pregnancy, surgery is the only modality to deal with intestinal obstruction and ectopic pregnancy simultaneously.

#### Surgical Treatment

The type of operation for intestinal obstruction depends on the severity of the obstruction. If simple, adhesiolysis is performed. Bowel resection is made if gangrene is present due to long-standing obstruction or strangulation. A decision on continuity or stoma is made on several factors, as in other causes of intestinal obstruction.

#### Gynecologic Treatment

The type of operation for ectopic pregnancy depends on the location of the ectopic pregnancy. The treatment of choice for unruptured ectopic pregnancy is salpingostomy, sparing the affected fallopian tube and improving future reproductive outcomes. Salpingectomy is performed if the Fallopian tube is morphologically changed to preclude further fertility (see Chap. 15).

### 18.12.3 Normal Pregnancy

#### 18.12.3.1 Historical Perspective

Pinard, in 1902, was quoted by LePage et al.: “*There is no need to begin another chapter in puerperal pathology entitled ‘Intestinal Occlusion of Pregnancy’. I have never seen intestinal occlusion complicate a normal pregnancy*” [419]. The explanations offered by the various French and German writers varied. The French writers discuss the anatomic causes in abdomens without previous surgical intervention and so without adhesions as far as is known. Sencert and Cuneo called attention to the intestinal occlusion caused by a loop of bowel caught and held by the infundibulopelvic ligament, the latter being held taut by a gravid uterus rising into the abdomen. Vautrin, of Nancy, in 1922, presented two cases of acute intestinal obstruction caused apparently by normal pregnancy [419]. Vautrin pointed out the “colic angulation” caused by the tense infun-



dibulopelvic ligament, the stercoral accumulation adding to the trouble, and the two causing obstruction. Ludwig, in 1913, assembled 96 cases of intestinal obstruction occurring during pregnancy. He found the condition most common in the 3rd and 4th months and again in the last 3 weeks of pregnancy [3]. These cases were perhaps partly aggravated by the pregnancy, but none could be directly attributed to the pregnancy alone. In 1918, Fleischauer [419] reported two intestinal obstructions during pregnancy—one, a woman pregnant 4 months with severe obstruction and peritonitis. At the autopsy, a hindrance to the passage of the intestinal contents was found at a point where the possibility of compression between the uterus and pelvic brim arose. There was also dilation of the ureters where they entered the pelvis, so in this case, the gravid uterus must be considered the cause of the obstruction. According to Fleischauer, this case confirmed the opinion of Van der Hoeven in 1912 that in the 3rd and 4th months of pregnancy, occlusion of the bowel is more liable to appear than at any other time, that is to say, at the time the uterus rises beyond the brim of the pelvis [419]. Der Verf thought that in the final analysis, the cause of the ileus is found in the bowel owing to muscle weakness and loss of muscle tone. A second case, by Fleischauer, appeared in the 6th month. Adhesions caused the obstruction from a previous operation—the growing uterus being simply the deciding factor in the cause of the ileus. In LePage et al.'s comprehensive treatise on the subject from 1913, the patients are divided into two classes [419]:

- Without any history of intestinal or peritoneal trouble,
- With a history of intestinal or peritoneal trouble and possible operation.

LePage et al. say: *If we can diagnose those exceptional cases in which the presence of a gravid uterus suffices to produce an obstruction, even occlusion, in an intestine non-adherent and*

*with no bands but simply compressed, therapeutics should immediately consist in getting rid of the uterine tumor.* This course, he adds, *raises the great question of the right of the fetus to life.* Köhler, in 1920, says the cases in which a pregnant uterus alone produces the ileus are rare [420].

### 18.12.3.2 Incidence

The incidence is extremely rare. A review of the literature up to 1926 by Bohler found only twelve cases published in a paper from 1930 [420].

### 18.12.3.3 Pathophysiology

The concept of pathophysiology is simple. The enlarged uterus causes compression in the locations where the bowel cannot move freely or where there are junctions of mobile and immobile parts of the bowel:

1. Rectosigmoid junction (pelvic brim),
2. Point where the bowel, in the form of a stoma, enters the abdominal wall,
3. Ileum proximal to the ileoanal pouch (J-pouch).

Ad 1. The rectosigmoid junction is the most common because the uterus is located in the lower abdomen in all phases of uterine enlargement. A possible additional factor is the long sigmoid loop predisposing to kinking and the development of sharp angles [421–423].

Ad 2. Theoretically, the incidence increases as the pregnancy advances due to enlargement of the uterus (both cases are after 32 weeks of gestation). In pregnant patients with normal bowel anatomy, the terminal ileal loops remain relatively mobile, allowing them to move aside when abutted by the enlarging uterus and maintain normal patency and function. The obstruction can have several similar mechanical

mechanisms. The enlarging uterus may also drag on the ileostomy loop from within, causing stomal retraction. Incarceration is a theoretical risk; it can arise either from adhesions fixing the retroverted uterus in the pelvis or possibly from the pernicious habit of rectal surgeons of using the uterus to close the pelvic floor after excision of the rectum. Stomal problems are common and are caused by displacement, enlargement, and sometimes prolapse. Fortunately, most of the abdominal wall stretching is in the region of the linea alba, and the stoma gets eased out of the way laterally. Additional nutritional support, such as oral iron, can provoke ileostomy dysfunction in patients with an ileostomy.

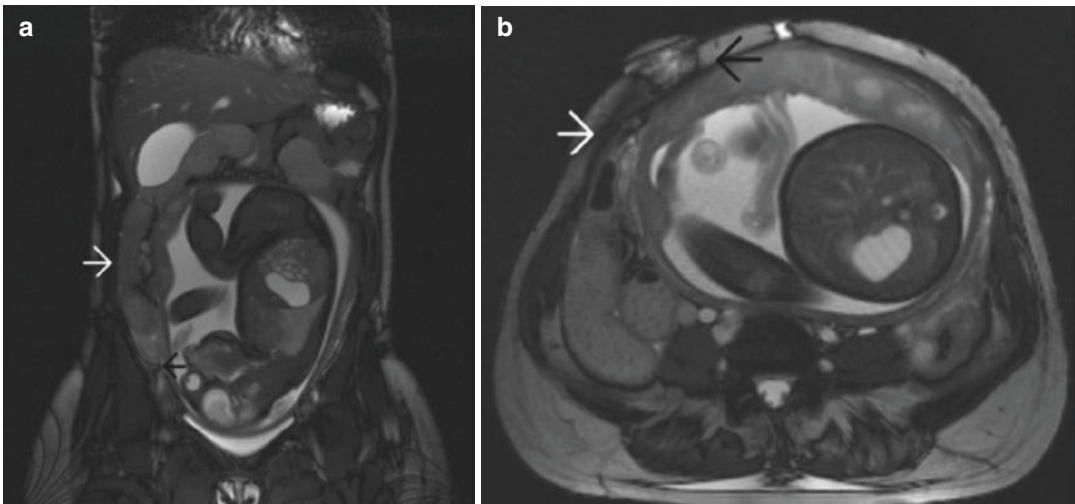
Ad 3. The explanation could be that ileum proximal to J-pouch is more or less tensed and cannot freely move away from the enlarging uterus, and therefore, obstruction occurs.

Some conditions should be fulfilled to diagnose *intestinal obstruction caused by normal pregnancy*:

- No obstructive symptoms before pregnancy except long-standing constipation,
- No other causes of obstruction intraoperatively,
- Compression of the enlarged uterus on the bowel at the site where the proximal distended bowel continues to the collapsed bowel,
- No other causes of stomal obstruction (a parastomal hernia, stenosis, or prolapse).

#### 18.12.3.4 Diagnosis

With suspected intestinal obstruction, a plain abdominal X-ray is commonly diagnostic and sufficient to indicate the emergent operation. MRI of the abdomen (with or without peroral contrast) is used in unequivocal cases (Fig. 18.59). Multiplanar images could demonstrate multiple loops of the dilated small intestine. The point of transition from distended to collapsed bowel can



**Fig. 18.59** (a) Coronal T2-weighted MRI shows dilated small bowel loops (*white arrow*) from the left upper quadrant down to the ileostomy in the right iliac fossa (*black arrow*); (b) axial MRI at the level of the stoma shows a change in caliber, (*white arrow*) from the dilated small

bowel to the collapsed bowel adjacent to the uterus indicating the compressive effect of the uterus as a cause of obstruction. (Reproduced with permission from [306] under the CC Attribution License)

be identified with or without focal lesions that can cause obstruction. MRI can delineate bowel wall thickening, mucosal abnormalities, or signs of a parastomal hernia [306].

### 18.12.3.5 Treatment

This extremely rare condition occurs when most babies are viable. It is suggested that when intestinal obstruction intervenes during a normal intrauterine pregnancy, the abdomen be opened, and the cause, if possible, be ascertained. If there are no causes of obstruction except bowel compression by the enlarged uterus, then CS should be performed. If there is a suspicion that intestinal obstruction is due to pregnancy, without strangulation, and present near term, the delivery should be started vaginally or by CS [423]. In pregnancy of <28 weeks, this obstruction can often be relieved by placing the patient in the knee–chest position and dislodging the uterus by rectal manipulation.

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# Symptomatic Abdominal Wall Hernia

# 19

## Abstract

A hernia is an area of weakness or complete disruption of the fibromuscular tissues of the body wall. Abdominal wall hernias are not common during pregnancy because these are commonly repaired before a planned pregnancy to avoid possible complications during gestation. Specific differential diagnosis in pregnancy is round ligament varicosities which disappear after pregnancy. Hernias can be symptomless or present with slight discomfort or pain. Such hernias are not life-threatening and should be controlled regularly during pregnancy. Conservative measures should include weight control, stool softeners, abdominal binders, and avoiding heavy lifting. After spontaneous delivery and uterine involution, elective hernioplasty is indicated. A clinician should recognize emergent presentations—incarceration, strangulation, and bowel perforation because surgical consultation and emergency operation are mandatory. There is still no consensus on an irreducible hernia during pregnancy, but complications during pregnancy outweigh semi-elective operation. (Incarcerated) gravid uterus in a hernia poses a problem due to a higher risk of fetal death or obstetric complications. Therefore, operative treatment is recommended, including simultaneous obstetric and surgical management.

Surgical repair of hernias is the most common general surgical procedure. More than 20 million patients worldwide undergo hernia repair each year [1]. As the world population grows, there is a continuous increase in the absolute number of hernias in pregnancy. Also, the average age of primiparas is rising. Therefore, there will be more pregnant women with hernias presenting in elective or emergent settings. Increased use of laparoscopic access could lower the incidence of this condition.

Hormonal changes and increased intra-abdominal pressure during enlargement of the gravid uterus increase the rate of the development and progress of abdominal wall hernias in pregnancy. Pathophysiology of increased intra-abdominal pressure during pregnancy is presented in Chap. 3.

## 19.1 Groin Hernia

### 19.1.1 Historical Perspective

Praxagoras (the third to fourth century BC) was credited with the first reported operation in the general population by relieving strangulated inguinal hernia [2]. Strangulated inguinal hernias are extremely rare in the later months of pregnancy. Gaudier, in 1894, stated that a strangulated inguinal hernia and pregnancy are incompatible



[3]. That is probably incorrect, at least partly, because many groin lumps first appearing in pregnancy are due to varicosities of the round ligament, which at first sight simulate an inguinal hernia. Also, there are cases of strangulated femoral hernias. Unna reports about a 37-year-old woman with a strangulated femoral hernia and gangrene of the intestine that required the creation of a stoma. Miscarriage occurs on the 15th day. Reavray and Jollivet reported cases in the third month of pregnancy with strangulated femoral hernias. Kelotomy. Abortion on the 21st day; death on 27th day. Mr. Canton reports a case of a strangulated femoral hernia in the fourth month of pregnancy. Kelotomy; miscarriage and death the same night. Dr. WB Fletcher of Cincinnati has reported two cases: one miscarried on the 10th day after kelotomy for a femoral hernia. His second patient was pregnant for 4 months and was operated on for a strangulated femoral hernia and miscarried 10 days later but recovered. Weiner operated 37-year-old woman with a femoral hernia, who was 3-month pregnant. She had a miscarriage on 3rd day but recovered. Chelius records three cases of strangulated umbilical hernia in pregnant women. Cooper's patient was in the 8th month of pregnancy, Lawrence's patient in the 8th month, and Clement's patient in the 3rd month. Kelotomy was performed in each case with recovery. Fothergill says, "The uterus occasionally is lodged in the sac of an umbilical, femoral or inguinal hernia, where it may become impregnated; in which case an abortion may be induced and the hernia reduced or hysterectomy may be performed" [4].

## 19.1.2 Incidence

### 19.1.2.1 General Population

The estimated lifetime risk of inguinal hernia repair is 27% for men and 3% for women in the general population [5]. In women, elective and emergent inguinal hernia operations have a bimodal age distribution: during the first 9 years of life and after 30 years. The incidence in women is 9–10 times less than in men. Only 9% of inguinal hernioplasties are performed on women; 7% are emergent [5]. In nonpregnant women, the

indirect inguinal hernia is 2.5 times more frequent than a direct hernia during elective operations (54.3% vs. 23.1%), while the difference during emergent operations is significantly smaller (23.5% vs. 17.2%). Elective femoral hernias comprise 15.9%, while emergent present 53.6% [6].

### 19.1.2.2 Pregnancy

In pregnancy, an inguinal hernia has a reported incidence of 1/1000–1/3000, with 50% [7] to 75% [8–10] occurring in multiparas. The predominant side was right (86%) [7]. The incidence of incarcerated/strangulated groin hernias in pregnancy is unknown but is at least 10 times lower due to several factors. First, patients with a hernia planning pregnancy undergo an operation before or after pregnancy, lowering the incidence of future pregnancies. The growing uterus blocks the entrance of intra-abdominal contents in the hernia sack. Also, before the era of ultrasound (US), many intraoperative findings were not hernia [11].

## 19.1.3 Etiopathogenesis and Risk Factors

Some authorities from the previous century stated that a preexisting hernia frequently disappears during the later months of pregnancy: *the reason being that the enlarging uterus pushes the intestines away from the inguinal ring and presently blocks access to them* [12]. Gurdieu, an obstetrician, stated that "there are two causes which dispose the pregnant female to a hernia, one is a relaxed, softened state of the muscle fibers, with an excess of fluid in the tissues, the other is the weight."

The risk factors (Table 19.1) are the same as in the general population, plus the increased intra-abdominal pressure due to an enlarging gravid uterus.

## 19.1.4 Clinical Presentation

A reducible or nonreducible groin lump, which demonstrates an expansile cough impulse, is diagnostic while excluding other causes of a lump. Palpation of hernia content can differentiate a

**Table 19.1** Risk factors during pregnancy for abdominal wall hernia

|                      |
|----------------------|
| Family history       |
| Collagen diseases    |
| Smoking              |
| Renal failure        |
| Chronic lung disease |
| Diabetes mellitus    |
| Steroid use          |
| Malignancy           |
| Malnutrition         |
| Cirrhosis            |
| Ascites              |
| Obesity              |

solid structure (greater omentum or uterine fibroid) from the intestine (gas sounds on pressure). The inguinal region is assessed by applying the Valsalva maneuver, which increases intra-abdominal pressure. The maneuver is performed when a person tries to exhale forcibly with a closed glottis so that no air exits through the mouth or nose, for example, in strenuous coughing, straining during a bowel movement, or lifting a heavyweight. There is severe abdominal pain with nausea and sometimes vomiting if incarceration occurs. Bowel incarceration results in severe vomiting, sometimes with the absence of stool and flatus is present. Fever develops if perforation due to distension or strangulation occurs. In such cases, redness of the overlying skin is due to the spread of infection through the abdominal wall.

**19.1.5 Differential Diagnosis**

There are many causes of groin swelling/mass (Table 19.2).

**19.1.5.1 Round Ligament Varicosities**

*Varices of the round ligament are often mistaken for an inguinal hernia*  
(Carroll Harris Verovitz CH, 1941 [18])

**Historical Remarks**

Carroll Harris Verovitz (Fig. 19.1), in 1941, first reported round ligament varicosities (RLVs) as a diagnostic differential to an inguinal hernia.

**Table 19.2** Causes of groin swelling/mass [13–17]

|                                        |
|----------------------------------------|
| Lymphadenopathy                        |
| Subcutaneous lipoma                    |
| Cyst in persistent processus vaginalis |
| Round ligament varicosities            |
| Round ligament stretch                 |
| Round ligament myoma                   |
| Inguinal endometriosis                 |
| Inguinal metastases                    |
| Lymphoma                               |
| Hematoma                               |
| Abscess                                |
| Mesothelial cysts                      |
| Cyst of the canal of Nuck              |
| Aneurysms/pseudoaneurysms              |
| Soft-tissue malignancies               |
| Cystic lymphangiomas                   |



**Fig. 19.1** Carroll Harris Verovitz (1891, Illinois—1956, Cleveland, Ohio) was a Demonstrator of Surgery at Western Reserve University, School of Medicine in Cleveland, Ohio. He was a member of many societies (Cleveland Academy of Medicine, Ohio State Medical Society, Cleveland Heart Society, Cleveland Diabetes Society, American Medical Association, Gold Key, University of Vienna). (Reproduced with permission from [19])

Dodd and Wright [20] described the two-part operation—the first part consists of the division of the tributaries of the long saphenous vein and

the second part of the division of the veins of the round ligament. Hodgkinson and Kroll [21] stated that “Vignes gave credit to Cruveilhier for first recognizing the inguinal vein syndrome and cited a case reported by Burch of an inguinal swelling caused by dilated veins of the round ligament which was initially diagnosed as an epiploic hernia. Burchi attempted radical surgery, discovering that the inguinal swelling was caused by a large RLV without a hernia sac. Recovery followed resection of the varices.” It is unsolved whether Vignes wrote about the Pégot–Cruveilhier–Baumgarten disease. It is a rare separate entity of spontaneous portosystemic collateralization in which the umbilical or para-umbilical veins are distended.

### Incidence

RLVs are rare and almost exclusive for pregnancy [22]. Their true incidence is unknown [15, 23, 24] because RLVs are underdiagnosed. It is probably due to the general opinion that pregnant patients should have some pain during pregnancy. McKenna et al. claim the incidence of 0.013% [13]. RLVs present most commonly during the second trimester of pregnancy [25]. Only 17% are present in the postpartum period [22]. The development site was on the right, followed by the left, and then by both sides in the ratio of 11:9:6 [22]. A European study found right-sided predominance (3:1) [25], while Asian studies revealed left-sided predominance [26, 27]. Jung et al. made the first report on RLV during pregnancy in Korea in 2010 [28]. RLV thrombosis is at least 10 times less common [22].

RLV thrombosis is more common during puerperium [29–32].

### Pathophysiology

Anatomically, the round ligament extends from the lateral uterus to the major labia containing veins, arteries, lymphatics, and nerves. RLVs are prominent veins within the round ligament and are more common in pregnancy, especially in the second or early third trimester, because preg-

nancy promotes increased venous flow and reduced venous tone [17]. Several mechanisms for the development of RLV exist. Physiologically, progesterone receptors naturally occur within the round ligament veins [23], and as progesterone levels increase during pregnancy, progesterone-mediated venous smooth muscle relaxation causes dilation of these veins. Furthermore, increased blood volume and cardiac output increase the venous return with advancing pregnancy, especially during exercise [33]. This and a gravid uterus cause relative impingement of pelvic veins, resulting in venous engorgement. With widespread connective tissue pathology and vascular disease, hemorrhoids (50%) and varicose veins (46%) commonly accompany pregnant patients with RLV [25]. Although RLV shares similar pathology with hemorrhoids and varicose veins, their diagnosis is underreported compared to these diseases [34]. Therefore, these conditions are probably not directly associated with RLV. They are not specific risk factors for RLV, even though the manifestation in the second and third trimesters may again point toward the influence of the gravid uterus on the pelvic blood flow. There was no increased rate of (1) higher birth weights, (2) a positive family history of hernias, or (3) soft-tissue disorders [25].

RLV in pregnancy has not been confirmed as a precursor of an inguinal hernia later in life [25].

### Clinical Presentation

The distinction between a groin hernia and RLV is difficult clinically because the symptoms and signs are similar. The patient complains of a lump and an aching feeling in the groin with both conditions. RLV results in pain in half of the cases [22]. Both swellings disappear on lying down and reappear on standing, provoked by increased intra-abdominal pressure with coughing or the Valsalva maneuver. However, it may return more gradually than a hernia and is less circumscribed. The reducibility of RLV is because these veins do not contain valves and, therefore, can be partially

empty. RLVs also transmit cough impulses because transmitted abdominal pressure leads to vein distension [16, 17]; a clue that may suggest RLV is in the coexistence of lower limb or labial varicosities. An RLV is dull on percussion and more closely resembles a hernia containing greater omentum than the bowel. The absence of varicose veins elsewhere does not exclude the diagnosis of an RLV. Both traverse the inguinal canal and can be reducible or irreducible. RLV most commonly presents with a groin bulge and mild discomfort (Fig. 19.2).

**RLV Thrombosis** If the pain is the predominant symptom, thrombosis of RLV (Fig. 19.3) or variceal rupture should be excluded [30]. Thrombosis of the RLV increases the resemblance between an incarcerated inguinal hernia and RLV. Thrombosis produces a firm, tender, irreducible swelling without a cough impulse, simulating a strangulated inguinal hernia [31].

### Diagnosis

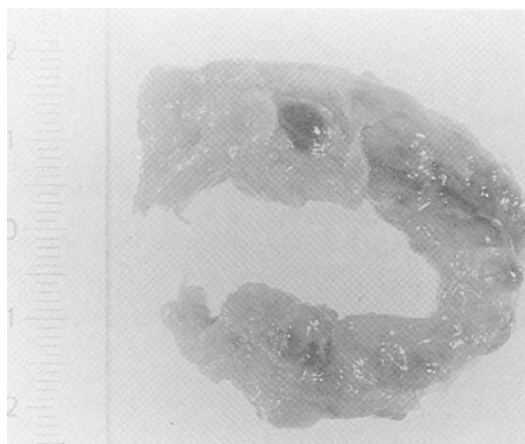
The US of the inguinal region can differentiate a multilocular mass (multiple echo-free serpentine tubular channels), which enlarges during the Valsalva maneuver (Fig. 19.4), from a single mass in a hernia, which also enlarges during the Valsalva maneuver. Peristalsis of the bowel

within a sac helps to differentiate it from RLV. The characteristic US appearances of varicosities simulating pelvic masses include (1) a prominent venous plexus with accompanying dilated draining veins passing through the inguinal canal, (2) veins draining into the inferior epigastric vein, and (3) the typical *bag of worms* appearances of smaller varices [31, 35] with the absence of bowel or lymph nodes in the inguinal mass [13]. Color Doppler US can confirm the venous flow and augmentation of this flow with the Valsalva maneuver (Fig. 19.5). Characteristic lymph node appearance is hypoechoic with an echogenic central hilum that demonstrates flow on Doppler imaging. The US appearance of endometriosis, hematoma, lipoma, or lymphadenopathy is not easily confused with RLV [24]. CT (Fig. 19.6) or MRI (Fig. 19.7) is indicated in doubtful cases, especially with accompanying abdominal pain.

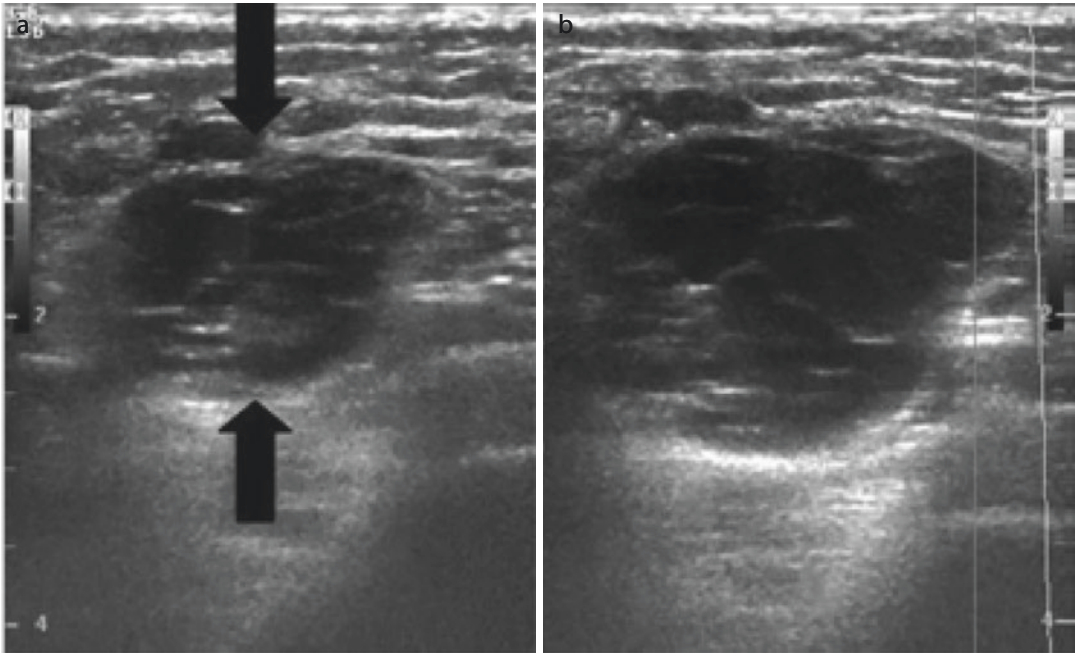
**RLV Thrombosis** Historically, the diagnosis of RLV thrombosis has relied on surgical evaluation [36]. However, US elements include noncompressible veins, no flow signal (Fig. 19.5c), and no intraluminal echogenic findings that suggest a thrombus. Even a clot can be visible within the lumen. Contrast-enhanced CT can reveal RLV thrombosis due to a lack of enhancement through the mass (Fig. 19.6). MRI can depict the local



**Fig. 19.2** Left inguinal swelling at 28 weeks of pregnancy (developed at 15 weeks) caused by round ligament varicosities. Note the *linea nigra* of pregnancy. (Reproduced with permission from [16])



**Fig. 19.3** The excised part of the round ligament, which is thickened with thrombosed varicose veins. (Reproduced with permission from [30])



**Fig. 19.4** (a) Transverse US of painful right reducible inguinal mass at rest shows a cystic mass (*arrows*). (b) Mass enlarged during the Valsalva maneuver. (Reproduced with permission from [2])

anatomy and has high contrast resolution, helpful in differentiating blood elements from a fluid collection or solid mass (Fig. 19.7).

### Treatment and Prognosis

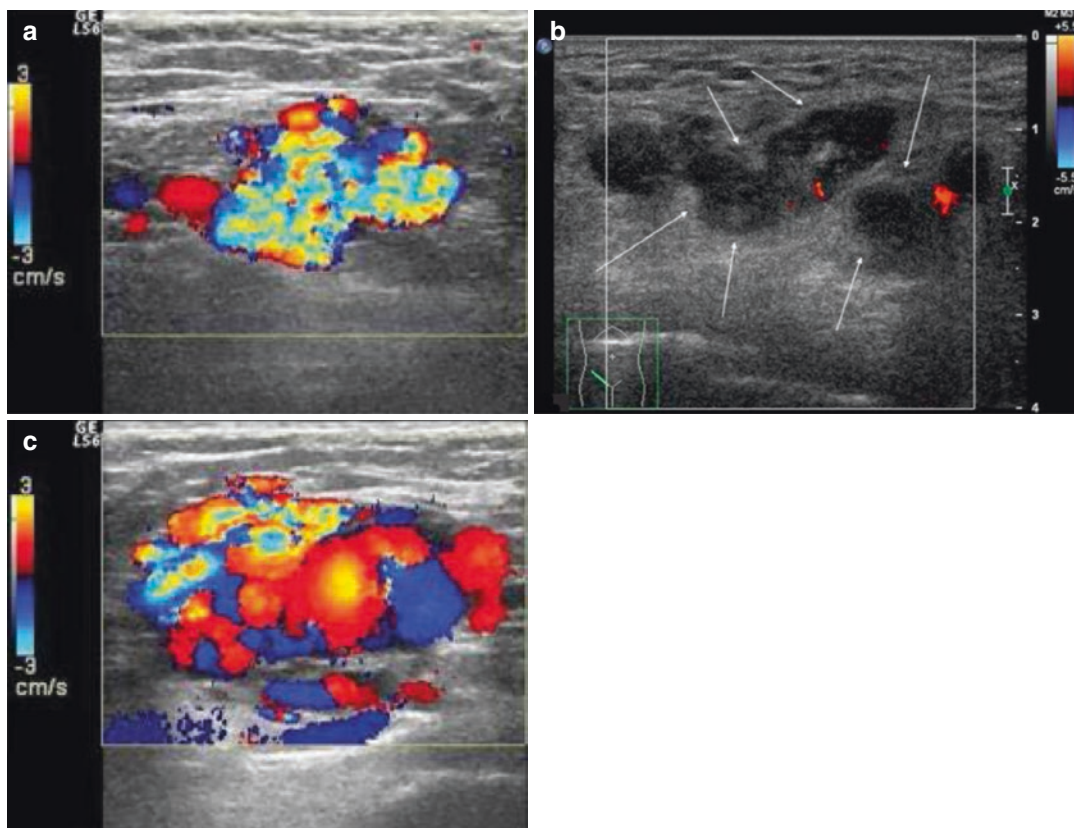
There is no specific treatment. Most symptoms resolve completely from 2 weeks [37] to 2 months postpartum [13], with 92.9% of RLV complaints subsiding within 4 weeks postpartum [25]. After delivery, when pelvic venous obstruction by the gravid uterus is relieved, spontaneous resolution, along with vulvar varicosities, will occur in most patients. A truss may, by giving support, add to the patient's comfort. Reassurance, with an explanation of the temporary nature of the lump during pregnancy and the recommendation of the usual supportive measures for the relief of vulvar and leg varicose veins, is all that is necessary. Recurrence of RLV is common, and most women will face symptoms in some (89%) or even all (83%) further pregnancies [25]. Nonoperative treatment is successful in >95% of cases [22]. Conservative treatment will not affect normal vaginal delivery. However,

RLV requires close monitoring during pregnancy as rupture and RLV thrombosis may result in intensely painful groin swelling.

A detailed description of the simultaneous surgical treatment of vulvar and RLV is from 1959 by Dodd and Wright. The patient is tilted into a 10° head-down supine position reducing the size of the veins and the bleeding. The incision extends from the anterior superior iliac spine to the pubic tubercle and curves to the thigh for 2.5 cm. The procedure consists of two steps (Fig. 19.8).

1. The saphenofemoral junction is defined. This requires division of the tributaries of the long saphenous vein, being the superficial external pudendal, superficial epigastric, superficial circumflex iliac, anterolateral, and posteromedial veins; the superficial external pudendal vein may be greatly enlarged. After ligating these veins, it is possible to open the foramen ovale and inspect the femoral vein, especially its medial aspect, for the deep external pudendal vein, which is present in 40% and may be





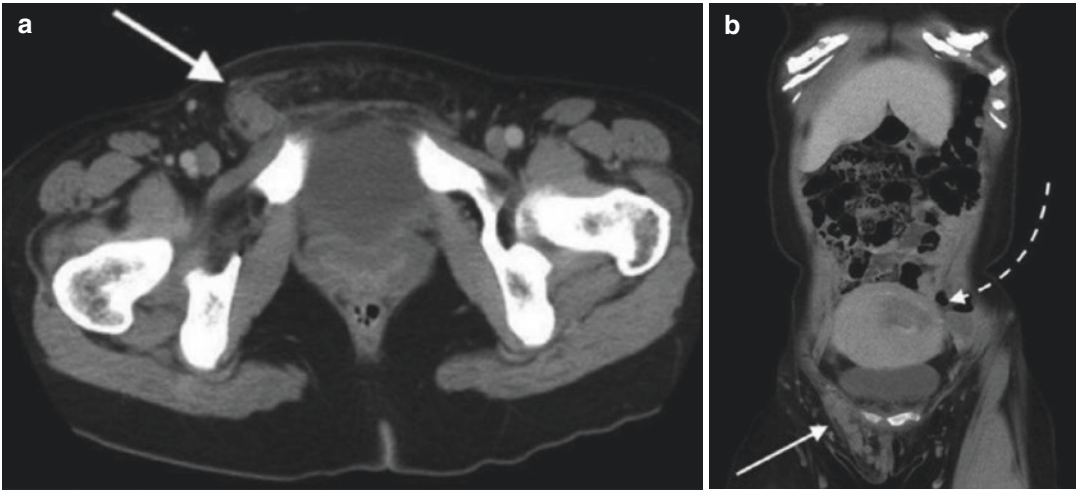
**Fig. 19.5** (a) Color Doppler US examination shows venous flow in the mass. (b) Valsalva maneuver caused marked enlargement and flow augmentation in the veins, consistent with round ligament varices. (Reproduced with

permission from [2]). (c) The right groin mass shows the absence of a Doppler signal within the vessels (white arrows), suggesting thrombosis. (Reproduced with permission from [31] under the CC BY 4.0)

varicose. It is ligated with thread. The saphe-nofemoral union is tied and transfixed,

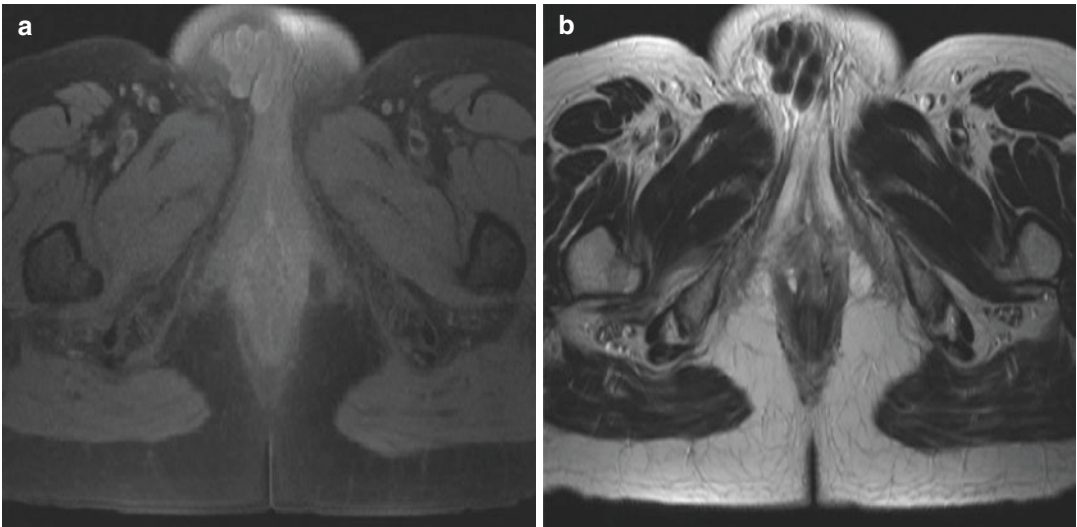
2. Veins of the round ligament are defined. The upper flap of the wound—that is, skin and subcutaneous tissue—is reflected to expose the surface of the external oblique and the external abdominal ring. The distended veins are visible as they enter the ring. The external oblique aponeurosis is split in the line of its fibers (as in a hernia operation) from the apex of the external ring to beyond the internal ring—that is, two-thirds of the way to the anterior superior iliac spine. The two leaves of the external oblique are reflected generously to expose the cremaster and conjoint tendon. A large vein from the superficial fat passes into the external ring and is divided between ligatures (hemostats tend to tear fragile vari-

cose veins). The upper leaf of the external oblique is wiped off the internal oblique toward the rectus abdominis muscle. The cremaster and bulky mass of veins and the round ligament are wiped off Poupart's ligament and the pubic tubercle until it can be elevated out of the inguinal canal on the finger. A large vein passing between it and the pubic tubercle is divided. The cremaster is separated along its fibers from the conjoint tendon above and divided just lateral to the internal ring until, with the round ligament, it is free from abdominal musculature; the cremasteric vessels are divided. The round ligament and its veins are drawn taut at the internal abdominal ring and divided with a secure ligature after transfixion. The large veins immediately shrink and become manageable; they have a



**Fig. 19.6** A right groin mass due to a thrombosed RLV on the 7th postpartum day. **(a)** Axial contrast-enhanced CT of the pelvis at the groin level shows a hyperdense serpentine structure (*white arrow*), extending from the right deep inguinal ring along the inguinal canal to the labia majora compatible with an RLV. Surrounding fat stranding is present due to thrombosis. A lack of enhance-

ment of the RLV supports the presence of thrombosis. **(b)** Coronal contrast-enhanced CT again illustrates the thrombosed RLV in the right groin with its course in the inguinal canal (*solid white arrow*). The gravid uterus (*dashed white arrow*) is seen. RLV: round ligament varicosities. (Reproduced with permission from [31] under the CC BY 4.0)

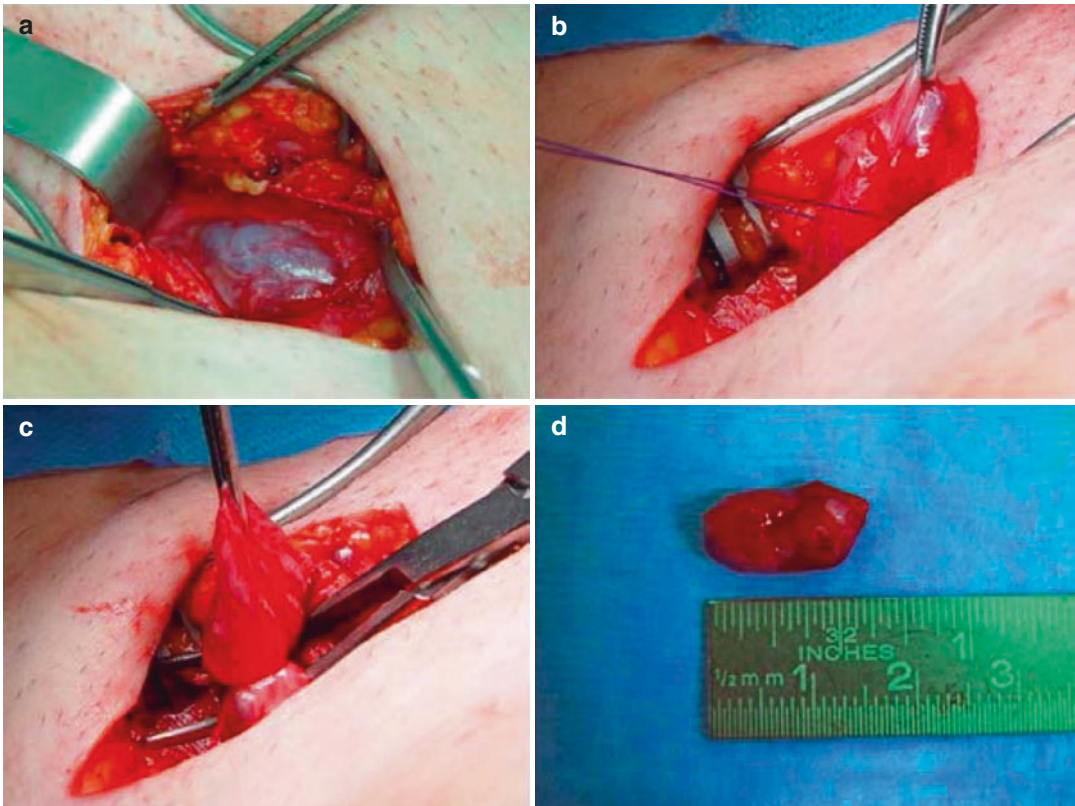


**Fig. 19.7** MRI shows a mass coursing from the right inguinal canal into the labium majus. The signal intensity of the mass was relatively higher than that of the muscle

on **(a)** T1-weighted images and very low on **(b)** T2-weighted images, suggestive of an acute or subacute hematoma. (Reproduced with permission from [32])

few connections posteriorly, including a considerable one at the medial border of the internal ring. This is divided. The mass is gently elevated, stroked clear from the fat below the

pubic tubercle, and drawn out of the labium major. Several vessels need securing in the process, and gradually, the mass of dilated veins emerges from the labia and is removed.



**Fig. 19.8** (a) Oblique incision in the left groin exposing varicosities of the round ligament, followed by (b) surgical exploration, and (c) ligation of the round ligament

with its varicose veins. (d) The excised specimen. (Reproduced with permission from [38])

**RLV Thrombosis** There is no consensus on management. Nonoperative management includes 6 weeks of low-molecular-weight heparin with follow-up Doppler US [31] or no treatment with spontaneous resolution [32]. Surgical exploration [29, 30] is recommended to (1) rule out a strangulated hernia and (2) reduce pain or discomfort caused by thrombosed RLV.

#### 19.1.5.2 Round Ligament Stretch/Pain

##### Pathophysiology

Physical exertion, sudden movements, or enlarging uterus pulls the round ligaments and stretches them (Fig. 19.9). The ligaments usually stretch easily, but occasionally growth rate is too fast, and small hematomas occur.

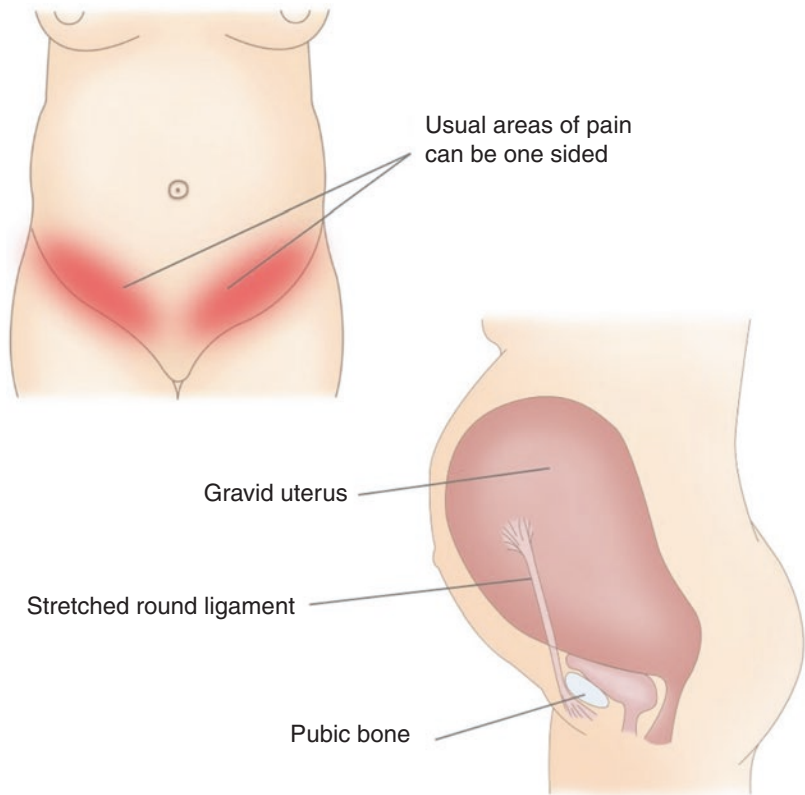
##### Clinical Presentation

Sudden localized abdominal pain around the hip area on one or both sides occurs with a constitutional upset. Pain can extend into the groin area. Tenderness is well localized over the round ligaments and sometimes radiates to their insertion along the inguinal canal and the pubic tubercle.

##### Differential Diagnosis

Other conditions with similar symptoms include AA, ectopic pregnancy, kidney stones, urinary tract infection, uterine contractions, inguinal hernia, ovarian cysts, and endometriosis. If abdominal pain is continuous and accompanied by vaginal bleeding, excessive vaginal discharge, fever, chills, or vomiting, then it is most unlikely to be RLP, and immediate specialist consultation is warranted [40].

**Fig. 19.9** Enlargement of the pregnant uterus causes distension of the round ligament producing abdominal pain. (Modified and reproduced with permission from [39])



### Diagnosis

Physical examination, blood and urine tests, and ultrasonography (US) exclude other causes of abdominal pain. Rarely was RLP diagnosed during exploratory surgery [16, 30, 41].

### Treatment and Prognosis

Treatment with analgesia, bed rest, and local warmth is curative in a few days.

#### 19.1.5.3 Inguinal/Round Ligament Endometriosis

Endometriosis is a uterine mucosa outside the endometrial cavity that can respond to ovarian hormonal stimulation. Abdominal wall endometriosis is any ectopic endometrium superficial to the peritoneum without association with a surgical procedure. Inguinal endometriosis is rare, with 0.3% of endometriosis treated in the general population. The incidence in the extraperitoneal part of the round ligament is 0.3–0.6% among women with endometriosis [42–45]. Most lesions

are right-sided; bilateral inguinal endometriosis is the least common [42, 44]. Right-sided predominance could be due to the coverage of the left groin by the sigmoid colon [46]. Also, the right inguinal predominance could be due to the peritoneal fluid's clockwise movement and the intestinal wall's peristaltic movement [47]. The mass diameter ranges from 1 to 6 cm [42, 43].

In 25% of published cases, inguinal endometriosis is associated with an inguinal hernia.

Cullen first reported endometriosis in the inguinal region in 1896, which he referred to as an “adenomyoma of the round ligament” [48]. Since then, less than 100 cases have been published. Theories of its origin include (1) congenital, (2) metaplasia, (3) metastasis, (4) implantation, and (5) direct extension of endome-



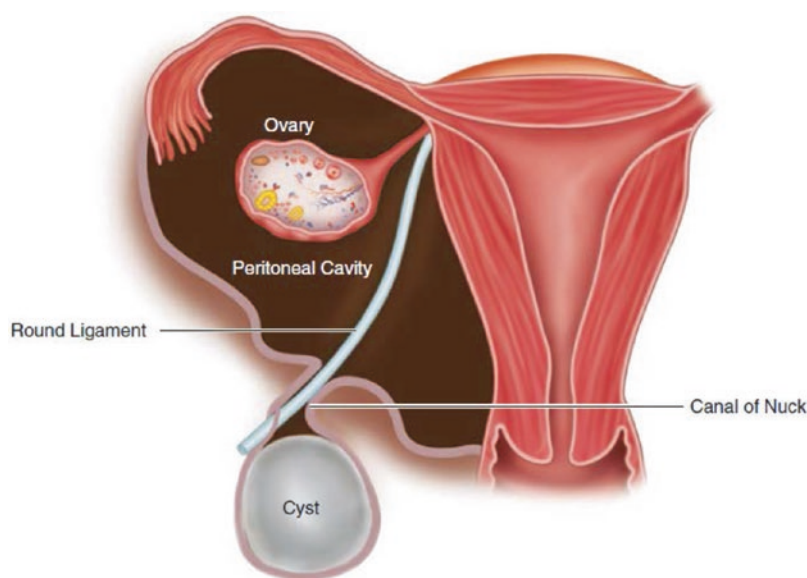
trial tissue along the round ligament [45]. The prevalence of round ligament endometriosis with deep infiltrating endometriosis is 13.8% [49]. The canal of Nuck, which is a small evagination of the parietal peritoneum that accompanies the round ligament through the inguinal ring into the inguinal canal, provides the most likely pathway for endometrial tissue to implant in the superficial inguinal soft tissue (Fig. 19.10) [50]. Endometriosis of the canal of Nuck could be a risk factor for ectopic pregnancy in a cyst of the canal of Nuck [51].

The symptoms commonly fluctuate with menses. Catamenial or cyclic pain is the pathognomonic symptom in the differential diagnosis of the inguinal mass. Unfortunately, only 57% of patients present with cyclic symptoms, which are not essential for the diagnosis. Another common symptom is bleeding from superficial lesions. Symptomatic complaints ranged from 3 months to 10 years, with an average of 3 years [42, 44]. Significant time delay exists between a patient's index surgery and the onset of symptoms in scar endometriosis. Patients develop symptoms on an average of 3.6 years. Despite fluctuating symptomatology, inguinal endometriosis should be included in the differential diagnosis because it is often diagnosed as an inguinal hernia preoperatively. Until the 1960s, correct preoperative diag-

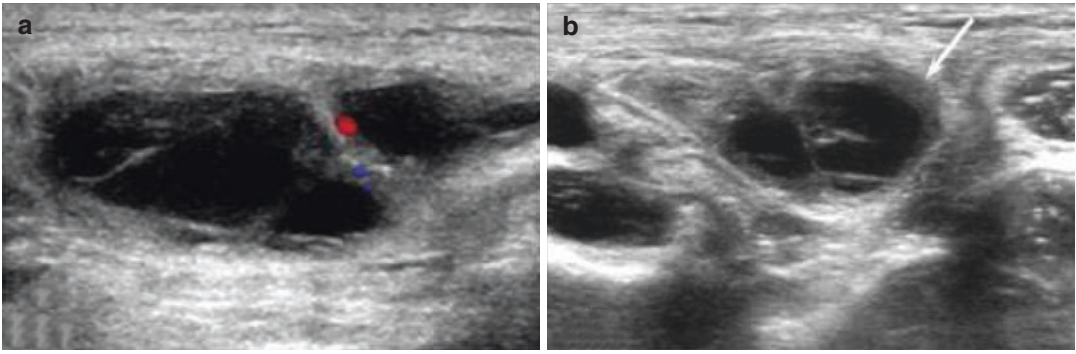
nosis was 25–35% (the inguinal US is not described) [45].

The US findings of inguinal endometriosis have been presented in <15 cases [46, 52–54]. The US features of inguinal endometriosis are variable: solid masses [52], cystic masses [46, 55], and combined cystic and solid masses [53]. Most cystic masses have internal septa (Fig. 19.11) [46, 49, 55]. These US findings differ from abdominal wall endometriosis near the Cesarean section (CS) scars. Most abdominal wall endometriosis findings are subcutaneous discrete nodules, hypoechoic with scattered hyperechoic strands and irregular, often spiculated, margins infiltrating the muscular fascia, circumscribed by a complete or incomplete hyperechoic ring caused by a perilesional inflammatory reaction (Fig. 19.12). No internal lesional vascularity or only internal lesional vascularity could be found on the color Doppler US. Lesions >3 cm and small cystic areas may be detected, possibly because of small blood lacunae of recent bleeding. Young et al. believe this difference is due to the different environmental situations between the two types of lesions. Inguinal endometriosis usually develops in the canal of Nuck, a cavity filled with fluid. If bleeding occurs within the implanted endometrial tissues, the canal of Nuck may be obliterated, and the structure may

**Fig. 19.10** Anatomic diagram of the canal of Nuck. The canal is a small evagination of the parietal peritoneum that accompanies the round ligament through the inguinal ring into the inguinal canal, providing the most likely pathway for endometrial tissue to implant in the superficial inguinal soft tissue

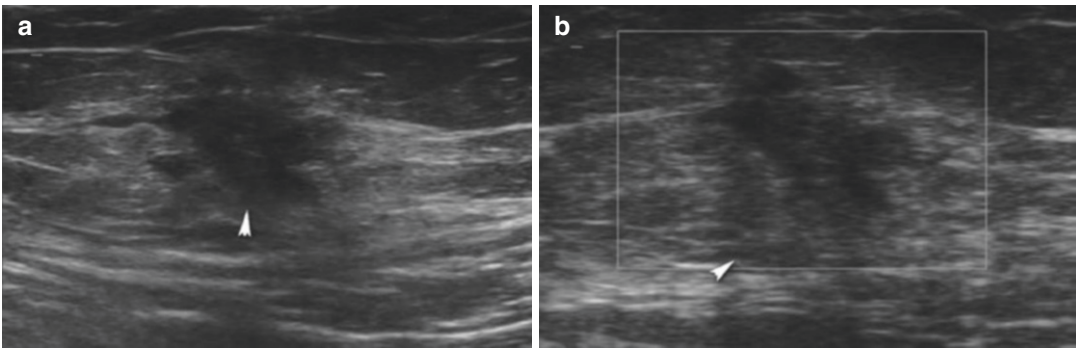






**Fig. 19.11** Imaging findings for inguinal endometriosis. Longitudinal color Doppler (a) and transverse gray scale. (b) US shows a cystic mass with an internal septum in the

right inguinal area (*arrow*). There are flow signals within the septum. (Reproduced with permission from [54])



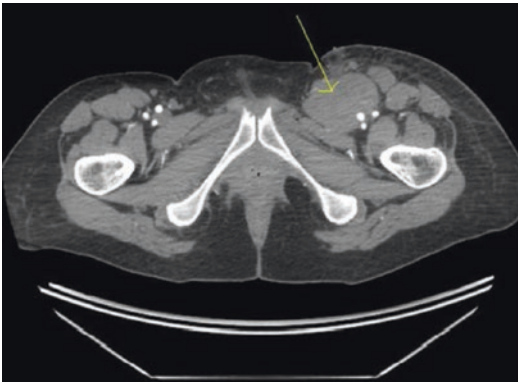
**Fig. 19.12** Abdominal wall (scar) endometrioma (*arrow*). (a) The transverse US shows an irregularly shaped, hypoechoic solid mass in the subcutaneous fat.

(b) Power Doppler US shows the absence of vascularization. (Reproduced with permission from [56] under the CC BY Attribution License)

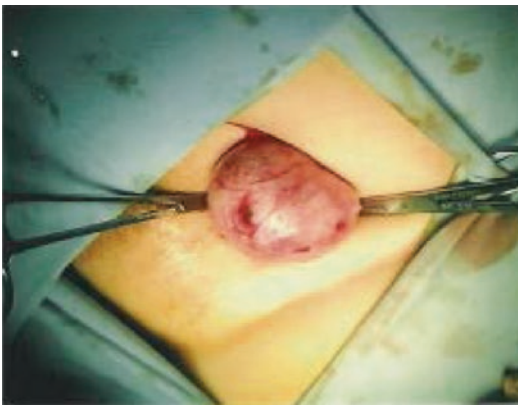
be vulnerable to the formation of a cystic mass. In contrast, cyst formation rarely develops in abdominal wall endometriosis because this lesion usually occurs in CS scars, which is a limited space compared to the canal of Nuck [49]. US-guided fine-needle aspiration (after ruling out abdominal wall hernia) is accurate for diagnosing inguinal endometriosis and excluding malignancy [57]. Computerized tomography (CT) of inguinal endometriosis shows a soft-tissue mass, mainly solid with the same density as muscle, and follows the course of the round ligament. In uncertain cases, magnetic resonance imaging (MRI) with a characteristic *shading sign* confirms an endometriotic nodule [58]. MRI shows the tumor size changes depending on the menstrual cycle, adding to the correct diagnosis [59].

However, in half of the reported cases of inguinal endometriosis, MRI features were not specific and included intermediate or high signal intensity on T2-weighted images [52, 59]. When inguinal endometriosis presents as a solid mass in US, the differential diagnosis includes neoplasms such as sarcoma, lymphoma, metastasis, enlarged lymph node, an abscess, and hematoma. Inguinal endometriosis as a cystic mass in the US should be differentiated from a hydrocele of the canal of Nuck (usually presents as a unilocular cyst [50] and an inguinal hernia).

A definitive diagnosis is made during the operation for inguinal hernia repair. The treatment consists of complete excision of the inguinal endometriosis, including the extraperitoneal portion of the round ligament (Figs. 19.13, 19.14 and



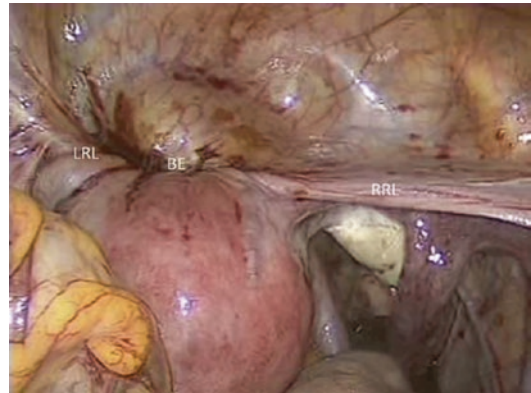
**Fig. 19.13** CT shows the left inguinal capsulated mass (arrow) in 35 weeks of pregnancy, confirmed as endometrioid adenocarcinoma arising from inguinal endometrioma. (Reproduced with permission from [60])



**Fig. 19.14** Right inguinal mass (endometriosis) during exploration. (Reproduced with permission from [47] under the CC BY Attribution License)



**Fig. 19.15** Gross specimen of right inguinal endometriosis. (Reproduced with permission from [47] under the CC BY Attribution License)

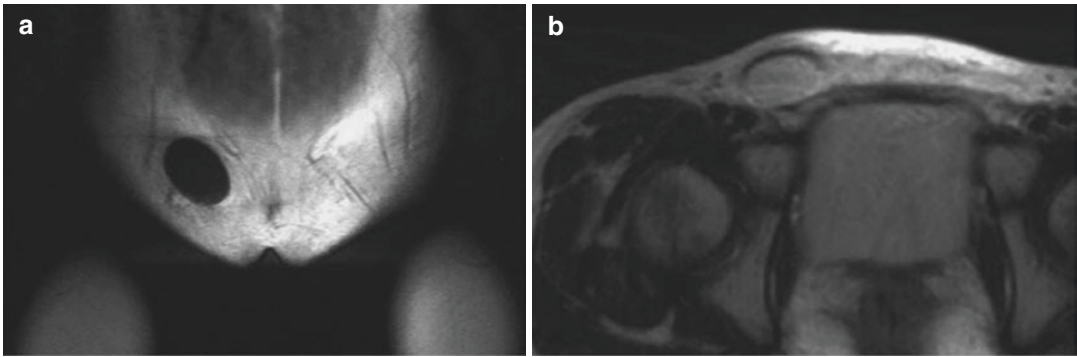


**Fig. 19.16** Round ligament of the uterus. *LRL*: a left round ligament that is shortened, widened, and deviated in the direction of the bladder due to endometriosis. *RRL*: a right round ligament thickened and pressured by a uterine deviation to the left. *BE*: bladder endometriosis. (Reproduced with permission from [49])

19.15). Otherwise, recurrences are frequent [61]. Intraperitoneal endometriosis is found in most patients. Many recommend pelvic laparoscopy for the endometriosis in the extraperitoneal part of the round ligament or a scar because of the association with pelvic endometriosis and subfertility (Fig. 19.16) [42, 43]. Approximately 13% with abdominal wall endometriomas had a history or subsequent diagnosis of pelvic endometriosis [62]. This percentage is within the overall incidence of pelvic endometriosis in menstruating females (8–15%) [63]. Hence, pelvic endometriosis in patients with abdominal wall endometriomas is within the same range as the general population.

#### 19.1.5.4 Hydrocele of the Canal of Nuck

The round ligament is attached to the uterus near the fallopian tube origin. A small evagination of the parietal peritoneum accompanies the round ligament through the inguinal ring into the inguinal canal [64]. This evagination of the parietal peritoneum in the canal of Nuck is homologous to the processus vaginalis in a male. The canal of Nuck usually undergoes complete obliteration during the first year of life. Failure of complete obliteration results in an indirect inguinal hernia. If obliteration fails in the distal portion of the canal, a sac containing serous fluid remains—the



**Fig. 19.17** MRI of a hydrocele of the canal of Nuck. (a) Coronal T1-weighted and (b) axial T2-weighted images show a thin-walled cystic mass in the right inguinal area. (Reproduced with permission from [50] under the CC Attribution License)

so-called *hydrocele of the canal of Nuck* [64, 65]. The hydrocele of the canal of Nuck is rare. It manifests as a painless swelling in the inguinal area and major labia. The cysts are usually small, averaging 3 cm in length and 0.3–0.5 cm in diameter [66]. US finding of a hydrocele of the canal of Nuck is typically sausage-shaped, extending along the route of the round ligament [65], or comma-shaped with a surface beak representing a continuation of the peritoneal cavity through the inguinal canal [50]. MRI shows a hydrocele of the canal of Nuck as a thin-walled tense cystic mass in the inguinal area (Fig. 19.17). During the operation, a cystic mass adjacent to the round ligament is found (Fig. 19.18). Complete excision, including the adjacent round ligament, is recommended because the definitive diagnosis is sometimes established only with pathohistological analysis.

#### 19.1.5.5 Myoma of the Round Ligament

The patients are usually aware of the mass in the groin before pregnancy or have been diagnosed with uterine fibromas before pregnancy. Untreated mass progressively enlarges. The growth is rapid during the first trimester of pregnancy due to increased levels of several hormones (see Chap. 12). The distinctive features of this inguinal protrusion are sharp borders, solid consistency, and rubbery texture. On coughing, a distinct impulse is transmitted. With recumbency, the prominence of the mass diminishes



**Fig. 19.18** A comma-shaped cyst with a surface beak continuing the round ligament extends the peritoneal cavity through the inguinal canal. The round ligament with tense cystic mass was excised. (Reproduced with permission from [50] under the CC Attribution License)

due to the recession of the mass into the inguinal canal.

### 19.1.6 Diagnosis

#### 19.1.6.1 Plain Abdominal X-ray

A plain abdominal X-ray confirms bowel obstruction due to incarcerated inguinal hernia in the general population. If bowel obstruction is not present, the part of the greater omentum is probably incarcerated. This imaging method is not mandatory because clinical suspicion of incarcerated inguinal hernia indicates an emergency operation. The transabdominal US excludes other causes.

### 19.1.6.2 Transabdominal Ultrasound

Hernias with characteristic clinical features need no additional investigation [67]. In pregnancy, many differential diagnoses are confirmed by grayscale or color Doppler US, and many are treated nonoperatively (see Sect. 19.1.5). Therefore, in pregnancy, the transabdominal US for groin swelling is mandatory. The US and Doppler US characteristics of the herniated bowel in inguinal hernia include bowel peristalsis, mucosal blood flow, or mesenteric fat [24].

## 19.1.7 Treatment

### 19.1.7.1 Conservative Treatment

During pregnancy, asymptomatic, reducible groin or umbilical hernias can safely be managed nonoperatively until postpartum. All of these patients have uncomplicated deliveries [7]. Gaudier, in 1894, stated that a strangulated inguinal hernia and pregnancy are incompatible [68]. Berkeley et al., in 1938 [69], and Baird, in 1950 [70], stated that preexisting hernia frequently disappears during the later months of pregnancy, “the reason being that the enlarging uterus pushes the intestines away from the inguinal ring and presently blocks access to them” [69].

The incarceration during pregnancy or delivery caused by a groin hernia with a previous symptomatic manifestation during pregnancy has not been described [71]. During pregnancy, a watchful waiting strategy is recommended in women with groin hernias [10].

Therefore, elective, postpartum hernia repair has similar results to the nonpregnant population [7]. A groin bulge resolves within several days after childbirth, and less than one-fifth underwent postpartum repair.

### 19.1.7.2 Surgical Treatment

Incarceration and persistent pain are indications for exploration during pregnancy. There are two

issues: (1) the use of prosthetic materials during pregnancy and (2) the role of the abdominal binder in the early postoperative period during pregnancy.

### 19.1.7.3 Gynecologic Treatment

RLV might have been misinterpreted as groin hernias, as not all patients had diagnostic ultrasonography [71]. Suspicion or proven incarceration mandates exploration [72]. Gynecologic consultation is mandatory for myomas in the hernia sac. Options are (1) bleeding, hematoma, or necrosis (degeneration) of uterine fibroids due to vascular insufficiency mandate excision and (2) uncomplicated uterine fibroid can be pushed into the abdomen and hernia repaired.

### 19.1.7.4 Inguinal Herniorrhaphy During Cesarean Section

Ferguson made one of the earliest descriptions of simultaneous surgeries in the general population in 1908 [73]. It was not uncommon to remove the uterus, salpinx, appendix, or prostate during a hernioplasty. In the 1980s, surgeons cautioned that simultaneous surgeries were associated with an increased risk of postoperative complication rates up to 50% more than single procedures [74]. Combining clean and contaminated surgery of hernioplasty and open prostatectomy may increase the risk of infection [75]. Advances in anesthesiology and surgical techniques, particularly minimally invasive methods, have made combined surgical procedures more popular in the general population.

Even in an elective setting, a dilemma exists on whether to perform herniorrhaphy in a pregnant patient with an abdominal wall hernia and an indication for CS. Altchek and Rudick reported the first combination of inguinal hernia repair with elective CS in 1987 [76]. CS can be completed through a single incision when an umbilical, inguinal, or incisional hernia (IH) after midline or paramedian laparotomy is present. The duration of simultaneous operations is <120 min [77]. The procedure is significantly prolonged in patients with bilateral inguinal hernia [9]. Prolonged operation increases wound infection rate (in the general population):



61–90 min operations with 4.0% as opposed to 91–120 min operations with 6.2% and 8.0% in operations >120 min [78]. In pregnant patients, simultaneous operations did not result in a higher rate of postoperative complications or hospital stay. CS with the repair of more distant hernias requires separate incisions and significant prolongation of operation.

Combined procedures with a single incision do not result in prolonged hospitalization or increased complication rates [77, 79].

No complications were recorded during the perinatal and follow-up periods. No recurrences were observed [9] or were extremely rare [77], although follow-up is not consistent.

The benefits are a 2-in-1 operation, single incision, single anesthesia, and single hospital stay valuable for the patient and hospital, cost, convenience, and avoidance of the separation of the mother from her newborn baby entailed by a separate operation. The length of full recovery is not different in the combined surgery patients compared with those who received a CS alone [80]. Patients expressed subjective satisfaction and recommended the combined procedure primarily because it saved time and obviated the need for childcare during reoperation.

### Surgical Technique

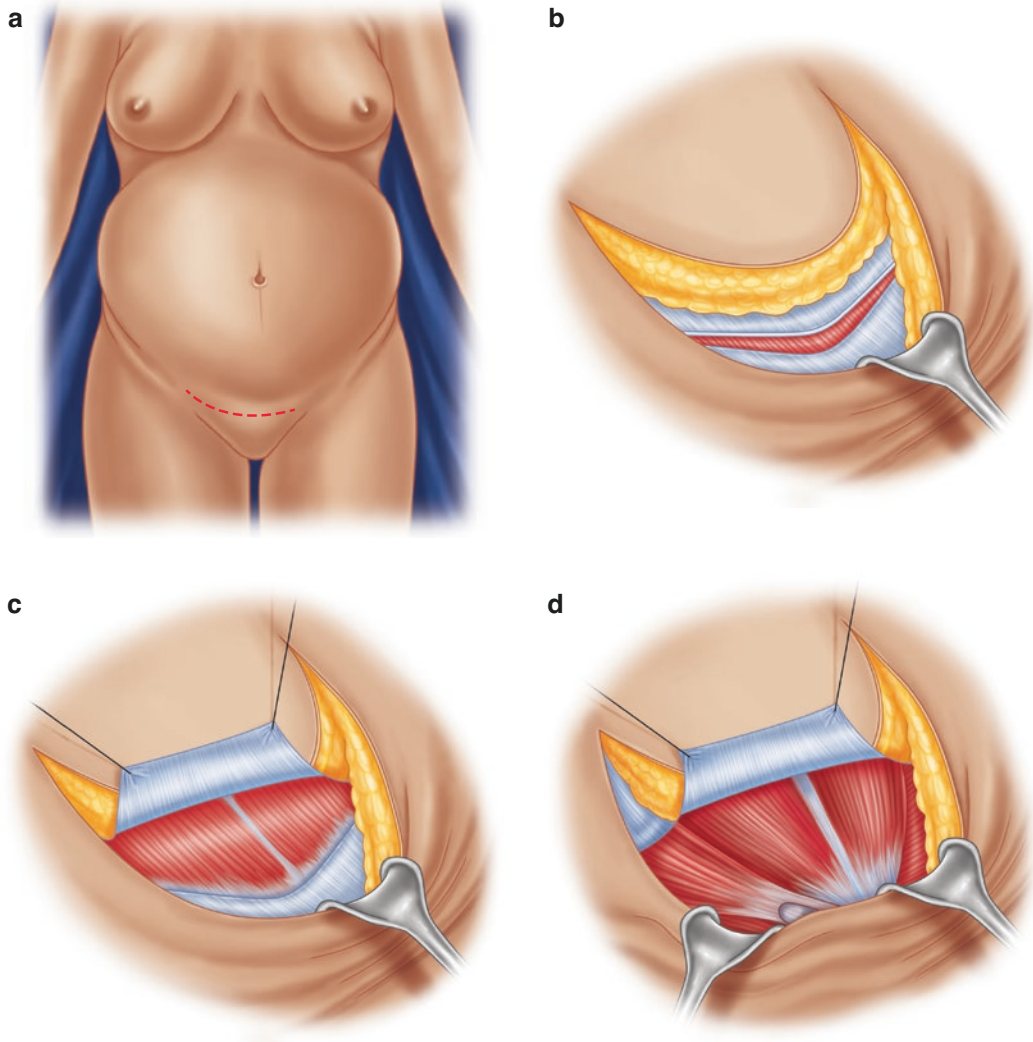
Simultaneous CS and inguinal hernia repair include a 10–12 cm Pfannenstiel incision along the pubic hairline centered over the pubic symphysis. The superficial and deep fascia is divided, exposing the rectus sheath. An incision is made in the rectus sheath with the parts directed superiorly and laterally at 30° from the skin incision, parallel to the inguinal canal, and up to the lateral border of the rectus muscle. The rectus and pyramidal muscles are exposed and separated in the midline (Fig. 19.19a–c), providing excellent exposure to the uterus. A standard CS is performed.

After delivery, a surgical team performs the anterior or preperitoneal inguinal hernioplasty.

*Anterior inguinal hernioplasty* is performed by dissecting the subcutaneous surface along the inferior aspect of the Pfannenstiel incision. The external oblique aponeurosis is exposed over the inguinal canal, and the superficial inguinal ring is identified (Fig. 19.19d). The external oblique aponeurosis is incised, and the inguinal canal is entered. The hernia sac is explored for indirect or direct hernias. There is no consensus on whether a tension-free Liechtenstein hernioplasty using a polypropylene mesh or Bassini repair is better. After mesh or Bassini hernioplasty, the external oblique incision is closed with a 3-0 absorbable suture [80].

During *preperitoneal inguinal hernioplasty*, the rectus muscle is retracted, and the preperitoneal space is dissected laterally, extending through the internal inguinal ring. While the Pfannenstiel incision is horizontally placed through the rectus abdominis sheet, it leaves the muscle intact and enters the peritoneal cavity between the left and right rectus abdominis muscles. There is no posterior rectus sheet at this level of the abdominal wall. Hence, retraction of the muscle enables direct preperitoneal access to Retzius space followed by the entrance in the space of Bogros. There are two reconstructive options after identifying a hernia and reducing its contents. The first is preperitoneal iliopubic tract repair [8, 76]. Continuous 2-0 polypropylene sutures should close to the posterior wall of the inguinal canal until the internal ring. A final one or two interrupted sutures are placed at the lateral edges of the ring. General or spinal/epidural anesthesia is used. The second is the preperitoneal placement of a 15 × 11 cm polypropylene mesh. Although the round ligament is an embryological remnant and is usually cut during the mesh placement, the lack of this ligament has been associated with uterine retroversion, which can cause chronic pelvic pain. For this reason, the round ligament is engaged from the keyhole, and the lateral keyhole interval was sutured and closed. Later, the mesh was fixed with a nonabsorbable 2-0 stitch to three points, the posterior rectus sheath, the pectineal ligament, and the anterior superior iliac spine, to prevent dislocation. The same procedure can be performed on





**Fig. 19.19** Schematic approach for the simultaneous Cesarean section and inguinal hernia repair. (a) Skin incision; (b) U-shaped incision on rectus sheath; (c) dissec-

tion of a superior leaflet on rectus sheath; (d) exposition of external oblique aponeurosis over the inguinal canal. (Reproduced with permission and modified from [80])

the other side for bilateral hernias. Finally, the wound is closed without using a drain [81].

### 19.1.8 Prognosis

The postoperative course of the incarcerated inguinal hernia depends on the content of the hernia sac and the duration of the incarceration. The essential late complication is hernia recurrence. No data exist about postherniorrhaphy pain or surgical site/mesh infection during pregnancy.

#### 19.1.8.1 Hernia Recurrence

Recurrence in the general population is 1–20% [82]. It is often secondary to a deep infection, undue tension on the repair site, or tissue ischemia. The high postoperative morbidity rate in nonpregnant women compared with men is due to their high proportion of femoral hernias and an increased risk for the emergency procedure in all types of groin hernias [6]. Because femoral hernias are more frequent in recurrent hernias than in primary hernias, femoral hernias may be overlooked during the repair of inguinal hernias.

Possible reasons for the high rate of emergency operation in femoral hernias are no or vague symptoms before incarceration, and diagnostic difficulties, even at incarceration [6]. Long-term recurrence rates are unknown for inguinal hernioplasty during pregnancy. Factors that could interfere with normal healing are the laxity of the abdominal wall and the presence of an enlarged, gravid uterus. Simultaneous inguinal hernioplasty with CS did not result in higher recurrence rates [9, 76, 81], or the recurrence rate was 0% [7, 8, 80]. It should be interpreted cautiously due to the small number of patients and short-term follow-up.

#### 19.1.8.2 Postherniorrhaphy Pain

Postoperative groin pain (inguinal neuralgia and inguinodynia) follows the distribution of the regional nerves, including the ilioinguinal, iliohypogastric, lateral femorocutaneous, and genital branch of the genitofemoral nerve. Nerve injury is usually due to the entrapment of a portion of the nerve with the mesh or sutures. There are no studies about postherniorrhaphy pain in simultaneous inguinal hernioplasty and CS operations. Some state no pain or a different sensation or tenderness at the surgery site [8, 80].

#### 19.1.8.3 Surgical Site/Mesh Infection

Wound or mesh infection is an uncommon postoperative complication but represents another etiology of recurrence. In specialized hernia centers, wound infection is <1%. With (nonabsorbable) mesh, most postoperative infections could be treated with antibiotics after the incision is opened and drained [83]. Mesh removal is rarely indicated. Studies with simultaneous inguinal hernioplasty with CS do not mention wound infections [7, 8].

a unique case of a woman who previously had four normal deliveries. The gravid uterus escaped through the abdominal wall and hung down below the knees, but a thick, broad pedicle projection passed through it into the abdomen. The case was seen by several of the most noted physicians of Holland, but none ventured to interfere. At term, violent uterine contractions sent the fetus through the abdominal portal and down, out, and alive through the natural passages. He followed up the contracting uterus, pressed it inside, and remained there. He writes that the point of the emergence of the hernia was not a normal canal but an opening through the muscles [4].

Ernest F. Robinson (Fig. 19.20) made the first modern description of an umbilical hernia in pregnancy in 1907 [85]. Coley and Hoguet described the first incarcerated umbilical hernia in the 7th month of pregnancy in 1918 [86].



**Fig. 19.20** Ernest F. Robinson (1872–1945) settled in Kansas City and became a chief surgeon for two railroad companies and, in 1905, joined the University of Kansas School of Medicine as a Professor of Surgery—an association that lasted until 1909. (Reproduced with permission from [84], with permission from the University of Kansas Medical Center Archives, Kansas City, Kansas)

## 19.2 Umbilical Hernia

### 19.2.1 Historical Perspective

In 1531, Nicolaus Pol, an Italian physician, removed a mature infant from a labial hernia. The mother died, but the newborn survived [4]. Sylvester Saxtorph, a Dutch practitioner, recorded

### 19.2.2 Incidence

Approximately 5–7% of all primary hernias in the adolescent/adult general population are umbilical [87]. An infantile umbilical hernia results from an abnormally large or weak umbilical ring that fails to close in an otherwise normal abdominal wall. The herniation is typically at the umbilicus, but it may be above (supraumbilical) or below (infraumbilical). The defect is covered by skin. The umbilical ring is not covered by fat. The adult umbilical hernia may result from untreated infantile hernias that fail to close spontaneously. Only 10.9% of adults with umbilical hernias recalled having hernias from childhood, with a male-to-female ratio of 1:1 [88]. Umbilical hernias (protrusions of >5 mm and diameters of >10 mm from the abdominal skin surface) are present in about 15% of pregnant West African women [89]. Among the tribes of the Plateau region of Northern Nigeria, umbilical hernias are very common, and many regard the protruding umbilicus as a thing of beauty. Some even proudly adopt the name "Mai cibi"—the possessor of an umbilicus [90]. The incidence in the developed world is 0.05–0.2% [8–10].

### 19.2.3 Etiopathogenesis

#### 19.2.3.1 Risk Factors

Adult hernias usually present as *de novo* pathology because of either an abdominal wall weakness or an increase in abdominal pressure (as in pregnancy), cirrhosis, ascites, obesity [87], or its combinations. Widening of the linea alba during pregnancy leading to a diastasis recti abdominis evokes pull forces on the umbilical ring, which might lead to symptomatic umbilical hernia [91, 92]. In some undeveloped or developing countries, the umbilical hernia is treated by applying traditional herbal medicines, which often cause inflammation, necrosis, and sometimes gangrene of the skin resulting in decubital ulcers, which may precipitate spontaneous rupture of a hernia [93]. The umbilical hernia persists in all these patients who had a clinical re-evaluation postpartum, and no spontaneous disappearance of the

hernia is recorded [10]. It is unknown whether the umbilical hernias developed before or during pregnancy.

Incarceration/strangulation depends mainly on the angle at which the long axis of the presenting part meets the plane of the hole. In congenital umbilical hernias, it is usually 90°, but in inguinal hernias, the angle is more acute. In acquired adult umbilical hernias, the hole is made by stretching the interdigitating fibers, and the resulting hole is unlikely always at right angles to the force producing it. Therefore, incarceration/strangulation sometimes occurs.

#### 19.2.3.2 Uterine Fibroids

Uterine fibroids can be pedicled or sessile. Most uterine fibroids have a pedicle, which can easily enter any hernia sac smaller than the hernial orifice. The hypothetical mechanism of the incarceration of fibroids without pedicles is as follows. Due to the limited mobility of such fibroids, the risk of incarceration is much lower than that of pedicled counterparts. The progression of pregnancy makes the fibroid displace cranially onto the anterior wall of the uterus. During this process, compression of the uterus in the posterior to the anterior direction in the abdominal cavity may cause fibroid entrapment in the umbilical hernial opening. The incidence of fibroids during pregnancy (see Chap. 12) is 1–4% [94].

#### 19.2.3.3 Gravid Uterus

Finding a gravid uterus in an anterior abdominal wall hernia is rare and is usually found in multiparous patients [9, 93, 95–97]. A gravid uterus in a wide umbilical hernia causes direct pressure and enlargement of the umbilical ring. When the uterus fills up a hernia and during further pregnancy enlarges, it becomes incarcerated in a hernia.

#### 19.2.3.4 Laparoscopic/Single-Port Surgery

The development of a postoperative hernia after supra-, infra- or transumbilical incisions from laparoscopic/single-port surgery can be mistaken for an umbilical hernia. It could be differentiated by history taking and evidence of surgical scars.

### 19.2.4 Clinical Presentation

The types of presentations include the following:

- Incarcerated umbilical hernia,
- Incarcerated gravid uterus in an umbilical hernia (Fig. 19.21),
- Skin ulceration/skin necrosis overlaying umbilical hernia (Fig. 19.21),
- An umbilical hernia with spontaneous skin rupture at the point of skin necrosis (Fig. 19.22).



**Fig. 19.21** A multiparous woman with a giant umbilical hernia with skin necrosis over the umbilicus in 38-week pregnancy presented in labor. She had vaginally delivered previous children. She had never had an abdominal operation. (Reproduced with permission from [96] under the CC BY 2.0)



**Fig. 19.22** Spontaneous rupture of large umbilical hernia with eviscerated vital omentum. (Reproduced with permission from [98] under the CC BY 4.0)

The last two presentations are the most common with the gravid uterus in the umbilical hernia. The diagnostic process has two parts. First is the definition of (incarcerated) an umbilical hernia itself, and the second is the definition of the contents of the hernia sac, both important for the type of treatment. Diagnosis is definitive if there is a dilated umbilical ring with or without contents in a hernia sac. With incarceration, symptoms depend on the incarcerated organ and the duration of incarceration. Incarcerated bowel causes vomiting, abdominal distension, and absence of stool and flatus passage (see Chap. 18); incarcerated uterine fibroid or greater omentum causes only pain and local tenderness. If the bowel becomes necrotic, perforation ensues into the surrounding tissue of the abdominal wall with erythema and edema of the skin overlying the hernia. This should be differentiated from skin ulceration/skin necrosis due to the long-standing pressure, usually from an enlarged gravid uterus (Fig. 19.21).

### 19.2.5 Differential Diagnosis

#### 19.2.5.1 Omphalitis/Periumbilical Abscess

History taking is essential because, in omphalitis, there is no previous hernia. With a periumbilical abscess, there is often a history of cleansing the umbilicus with small sticks that cause skin abrasions with inoculating bacteria. Furthermore, systemic symptoms are rarely present with omphalitis or periumbilical abscess.

#### 19.2.5.2 Umbilical Endometriosis

##### Incidence

Cutaneous EM (CEM) accounts for less than 5.5% of all EM cases [99–101]. Primary or spontaneous CEM appears without prior surgery and includes <30% of CEM cases [99–101]. Cutaneous EM of the umbilicus is also known as *Villar's nodule* after the physician who first described it in 1886. Cutaneous EM can develop spontaneously during pregnancy, and umbilical



location is the most common [102, 103]; it may regress spontaneously after delivery [103]. Umbilical EM (UEM) accounts for up to 30–40% of all CEM cases [99, 100]. Until 2008, 234 cases of UEM have been described, only two in pregnancy [102, 103].

### Clinical Presentation

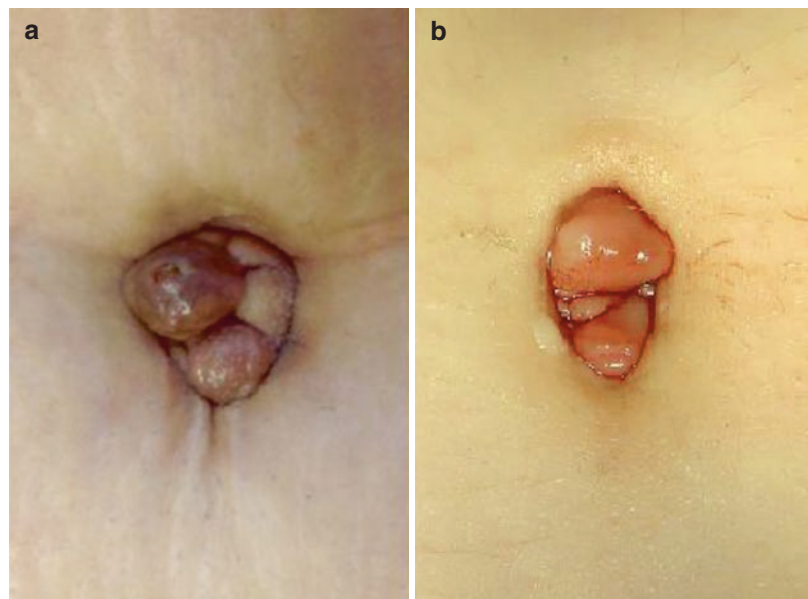
It manifests as a rubbery or firm nodule ranging from mm to 6–9 cm (mean 2–2.5 cm). Its color varies from red and blue to brown-black, depending on hemorrhage intensity and ectopic endometrial tissue penetration depth. Occasionally, the nodule is flesh-colored [104]. It is usually single and often multilobulated (Fig. 19.23), although multiple discrete nodules may be present [106]. Clinical symptoms include tenderness, pain, bleeding, swelling, and growth correlated with the menstrual cycle. However, not all symptoms are present in a given patient, and some are asymptomatic [107]. Cyclicity is not always demonstrable and is not essential for diagnosis [108]. Umbilical EM may be associated with an umbilical hernia [109, 110]. UEM associated with pelvic EM may present symptoms such as dysmenorrhea and dyspareunia.

### Diagnosis

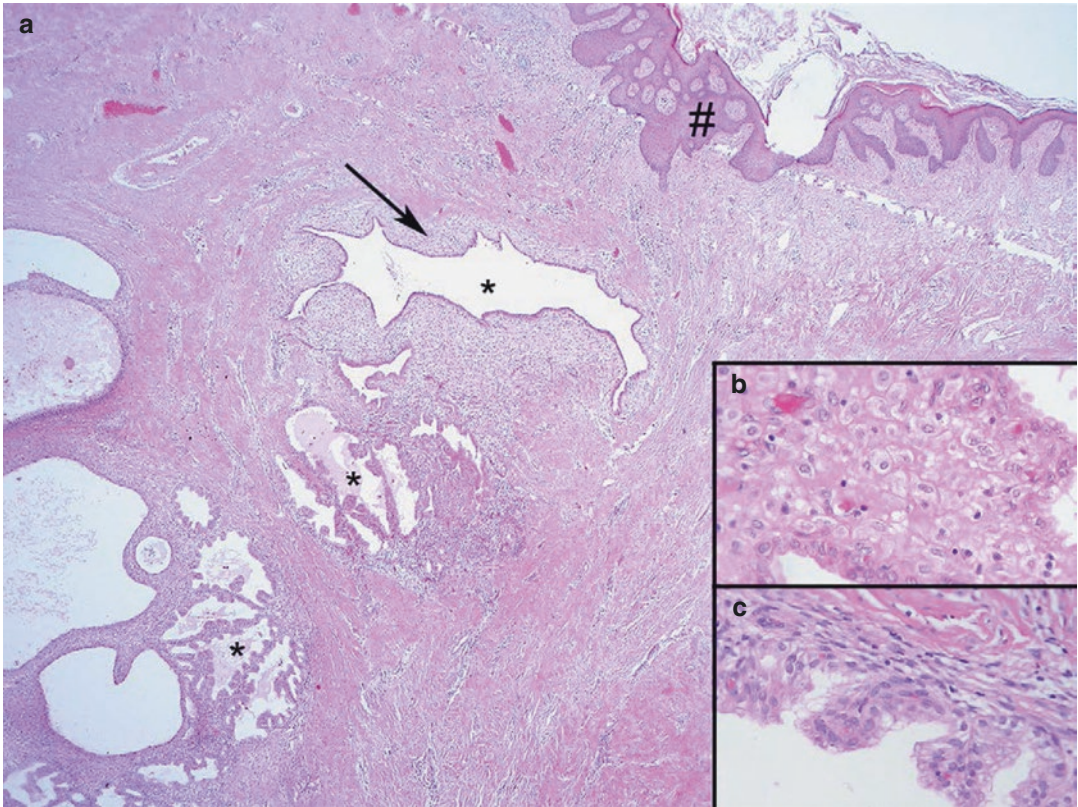
CEM diagnosis can be suspected clinically but relies mainly on histopathological examination (Fig. 19.24). Other helpful imaging methods include dermatoscopy, US, and MRI. Dermatoscopy of EM includes a homogeneous reddish pigmentation with small, well-defined, globular structures of a deeper hue, termed *red atolls* [111]. MRI findings include a low signal on T1 weighting and a low or high signal on T2 weighting, depending on the presence or lack of hemosiderin [107]. US and CT are not as sensitive as MRI. Fine-needle aspiration cytology results may be inconclusive [47, 101]. Serum CA-125 levels may be increased [103] but are not specific for EM.

Gynecologic examination and hormonal evaluation before CEM excision could detect an associated pelvic EM. Abdominal and transvaginal US or abdominal/pelvic MRI should be performed in all asymptomatic patients [47, 101, 104, 112] because extrapelvic endometriosis occupies various organs, and 15% of the patients present with endometriosis [99, 113]. Up to 40% of patients with extragenital endometriosis present with UEM.

**Fig. 19.23** (a) A multilobulated, red-brownish nodule over the umbilicus lasting 10 years, 2 years after the delivery of a single healthy baby. (Reproduced with permission from [105] under the CC BY Attribution License); (b) Caucasian, a nulligravid woman without previous endometriosis or umbilical operation. (Reproduced with permission from [102])







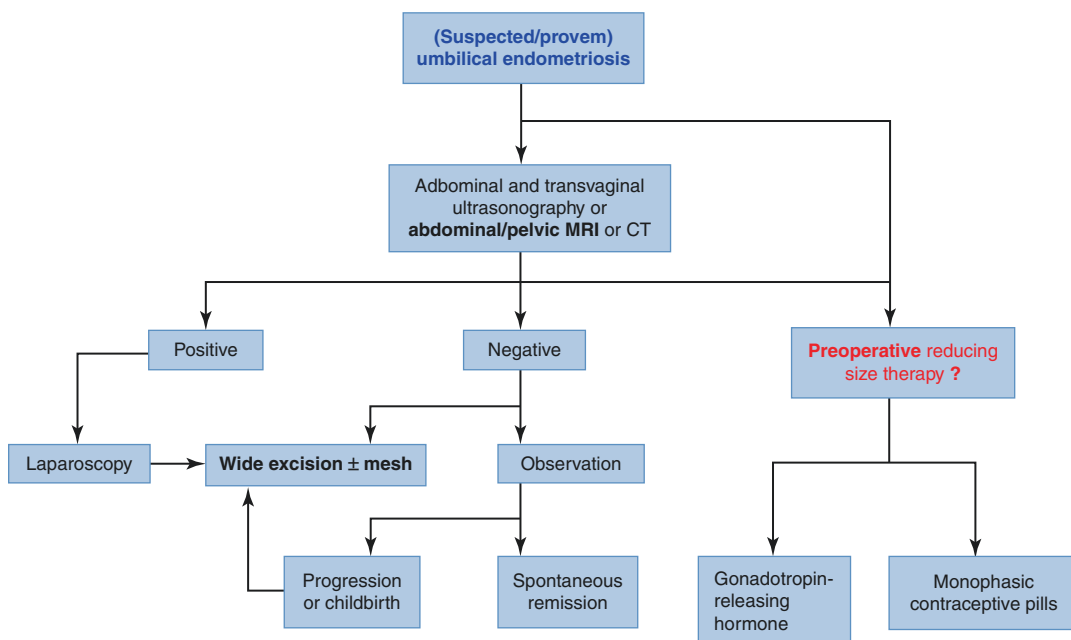
**Fig. 19.24** Endometriosis of the umbilicus. (a) The partial decidual reaction of the stroma. Histologic examination demonstrated endometrial glands (\*) surrounded by endometrial stroma (arrow) beneath the squamous epithelium of the skin (#) (hematoxylin and eosin  $\times 10$ ). (b)

Gestational hyperplasia and (c) focal Arias-Stella reaction of the endometrial epithelium as signs of pregnancy (hematoxylin and eosin  $\times 200$ ). (Reproduced with permission from [102])

### Treatment

CEM treatment in the general nonpregnant female population is mainly surgical (Fig. 19.25), preferably performed at the end of the menstrual cycle when the lesion is small to achieve a minimal excision [114]. The procedures vary depending on the size and extent of the lesion, from simple excision with wide margins (Fig. 19.26) under local anesthesia to laparoscopic excision en bloc of the umbilicus [104] with concomitant pelvic surgery for pelvic EM. A polypropylene mesh prevents the development of a hernia if the defect in the rectus sheath is large [101]. In the nonpregnant population, treatment with gonadotropin-releasing hormone agonists, danazol, and monophasic

contraceptive pills can reduce tumor size before excision or relieve the symptoms [99, 112]. These treatments are insufficient as sole treatments [112] and may lead to incomplete excision [101]. Whether laparoscopic examination for extrapelvic endometriosis should be systematically performed is still debated [47, 101, 104, 112]. There are no guidelines for pregnant patients [115], but these principles should be applied to the pregnant population except for adjunctive hormonal therapy, which is questionable during pregnancy. If pregnancy is advanced without significant progression of significant pain, bleeding, or enlargement, the treatment can be delayed after delivery due to the benign nature of the disease.



**Fig. 19.25** Treatment algorithm for umbilical endometriosis. During pregnancy, preoperative hormonal therapy is questionable and has not been studied yet



**Fig. 19.26** Completely excised endometriosis of the umbilicus. (Reproduced with permission from [102])

## Prognosis

The prognosis of CEM in the general female population is good. Recurrences are uncommon if excision is performed with clean and wide margins. However, malignant transformation has been reported in 0.3–1% of scar EM and should be suspected in the case of rapidly growing or recurrent lesions [116]. The most common histological subtype in malignant transformation is endometrioid carcinoma (69%), followed by clear-cell carcinoma (13.5%), (adeno)sarcomas (11.6%), and serous carcinoma [116]. The prognosis is unknown due to the minimal number of cases in pregnancy, while published cases claim excellent results [102, 103].

### 19.2.5.3 Umbilical Endosalpingiosis

Endosalpingiosis is rare. It presents the ectopic growth of the Fallopian tube epithelium [117]. Endosalpingiosis, endometriosis, and endocervi-

cosis constitute the triad of nonneoplastic disorders of the Müllerian system. These pathologies could be isolated but are more commonly associated with one another. The term endosalpingiosis was employed first by Sampson et al. in 1930. Under that term, the authors designated any unusual growth and invasion of the tubal epithelium in tubal stumps after previous salpingectomy or tubal sterilization [117]. There are no published cases of umbilical endosalpingiosis during pregnancy.

### Pathogenesis

The theories of endosalpingiosis are similar to endometriosis. Those two entities, together with endocervicosis, constitute the nonneoplastic disorders of the Müllerian system. One theory is based on the fact that endometrial cells (or their precursors) are transported by various routes (transtubal, hematogenous, lymphogenous, or direct apposition) and implanted in the affected organ. The other theory suggests that Müllerian ectopias result from metaplastic processes in the target organ (coelomic metaplasia theory, secondary Müllerian system) or scattered embryonic rest [118].

### Clinical Presentation

These lesions appear as nodules of the umbilicus and are usually brownish. The main symptoms (besides the esthetic) are pain and size fluctuation with menstruation. The lesion can be present after gynecologic procedures [119] or spontaneously [120].

### Diagnosis

The diagnosis is histological. In the case of endosalpingiosis, pathology confirms a tube-like epithelium containing three types of cells: ciliated, columnar cells; non-ciliated, columnar mucous secretory cells; and the so-called “intercalary” or “peg” cells [119].

### Treatment

The treatment of choice is surgical excision. Excision should be done under local anesthesia to minimize morbidity and hospitalization if small. However, laparoscopy should exclude

abdominal endometriosis with recurrent abdominal pain (especially in the lower quadrant).

## 19.2.6 Diagnosis

### 19.2.6.1 Plain Abdominal X-ray

A plain abdominal X-ray reveals bowel obstruction. A clinical diagnosis of an incarcerated umbilical hernia avoids ionizing radiation, eliminating the risk of fetal exposure.

### 19.2.6.2 Transabdominal Ultrasound

The transabdominal US excludes other etiologies of painful periumbilical lumps (see Sect. 19.2.5) or confirms the bowel in the hernia sac. Incarcerated uterine fibroid presents as a firm, hypoechogenic mass within the umbilical sac (Fig. 19.27).

## 19.2.7 Treatment

### 19.2.7.1 Indications and Timing

The timing of the operation is crucial. The emergent operation is an extreme rarity. In a population-based study, none of the identified women with a hernia required repair before childbirth [10]. Pregnancy after umbilical or epigastric hernia repair is associated with a 1.6-fold increased reoperation rate for recurrence [122]. The magnitude of this association is likely under-



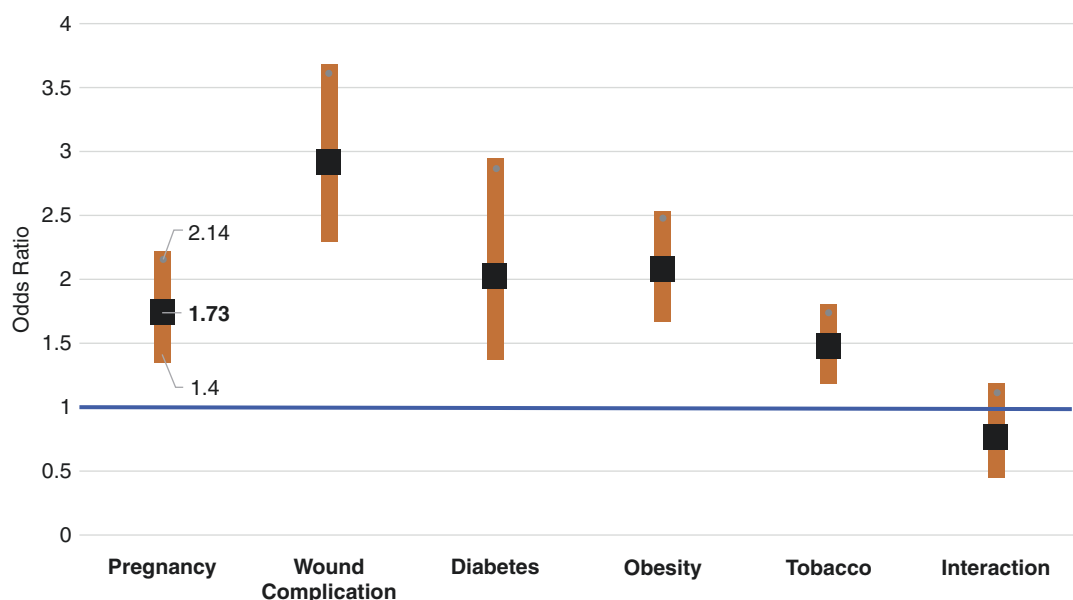
**Fig. 19.27** Transabdominal US at 32 weeks of the first pregnancy shows a hypoechoic, heterogeneous mass (uterine fibroid) 28 × 21 mm within the umbilical hernia sac. (Reproduced with permission from [121])

estimated, given that the risk of recurrence was defined as reoperation, which captures only the most clinically significant group of recurrences [123]. Therefore, pregnancy is the risk factor for hernia recurrence, with an odds ratio between tobacco smoking and obesity (Fig. 19.28).

This is similar to the repair of prepregnancy incisional or ventral hernia [71, 123, 124]. In contrast, the number of previous births at the time of repair of a primary ventral hernia does not influence the recurrence incidence. Thus, the accelerated abdominal distention during pregnancy is pivotal for hernia reformation rather than parity before the repair, albeit associated with an increased prevalence of lasting abdominal rectus diastasis [125]. No consensus exists on how long to postpone the hernia repair after delivery, but some recommend at least 1 year [126]. Electromyoneurographic changes in abdominal wall muscles return to the prepregnancy state after at least 8 weeks (see Sect. 19.6.1). However, some patients underwent surgery at 8–52 weeks postpartum with no complications or recurrence recorded in follow-up for 2–34 weeks [7]. The treatment algorithm for the pregnant population is the same as for epigastric hernia (Fig. 19.35).

Therapeutic goals consist of several parts. First is the management of hernial contents, which can be of various origins and sometimes need additional treatment. The second is the treatment of a hernia itself, and the third is to treat the cause of the herniation as applicable. Incarceration and strangulation are considered relatively uncommon, but when they do occur, these complications are responsible for 10–20% of the indications for umbilical hernia repair [128]. One of the first published cases of strangulated umbilical hernia in pregnancy was by Coley and Hoguet in 1918 [86] and ruptured umbilical hernia during pregnancy by Bruce Kenneth Young (Fig. 19.29) from 1965 [128]. Umbilical hernias in adults do not close spontaneously; slow enlargement over the years is common, and strangulation is much more frequent than in pediatric umbilical hernias. Therefore, an elective operation is mandatory for a presentation in the adult population.

As in the general population, the recurrence rate correlates with the body weight and width of the hernia orifice. In the general population, a mesh repair is used when the hernia orifice is >1 cm [130], decreasing the recurrence rate. In contrast, the mesh was not protective against



**Fig. 19.28** Risk factors of hernia recurrence in relation to pregnancy. (Reproduced with permission from [123])





**Fig. 19.29** Bruce Kenneth Young from NYU Langone Medical Center published one of the first cases of ruptured umbilical hernia in pregnancy. (Reproduced with permission from NYU Langone Medical Center webpage [129])

recurrence in women with subsequent pregnancies [122]. A repair with mesh may restrict the flexibility of the abdominal wall [131] and cause pain during a subsequent pregnancy [132]. The American College of Surgeons National Surgical Quality Improvement Program revealed 126 pregnant women with umbilical hernia repair in 10 years [17]. Ninety-five percent of the repairs used the open technique [133].

*Elective umbilical and epigastric hernia repair should, if possible, be postponed until after pregnancy and preferably until after the last pregnancy in women of childbearing age. If hernia repair cannot be postponed until after the last pregnancy, a sutured repair is suggested for umbilical and epigastric hernias in women of childbearing age. A mesh repair could be performed after the last pregnancy. (European Hernia Society, American Hernia Society [134]).*

These recommendations are later confirmed [135, 136].

Irreducible umbilical hernias without symptoms should be repaired semi-urgent before the enlarging uterus can potentiate organ (most commonly small bowel) strangulation. An irreducible symptomatic umbilical hernia is an absolute indication of an urgent operation. Skin ulceration without incarcerated hernia is a semi-urgent situation when frequent controls are necessary, and if progression to skin necrosis or skin rupture develops, the urgent operation is mandatory (Figs. 19.21 and 19.22). Six emergent suture repairs and one mesh repair of the umbilical hernia had no postoperative complications or recurrences [79].

Small incarcerated umbilical hernias without bowel obstruction can be operated on under local anesthesia minimizing the rate of anesthetic effects on both mother and fetus.

The role of the abdominal binder during the postoperative period in pregnancy and puerperium is unknown.

### 19.2.7.2 Umbilical Hernioplasty During Cesarean Section

The practical benefits are a 2-in-1 operation, with a single incision, single anesthesia, and single hospital stay, conferring valuable advantages for both patient and hospital in time, cost, and convenience, not to mention avoiding the separation of mother from newborn entailed by reoperation. Combined hernioplasty could be done with elective or emergent CS. Most umbilical hernia repairs are combined with elective CS [79]. In 2004, Ochsenein-Kölble et al. reported the first case series of CS and simultaneous umbilical hernia repairs [9]. Surgical options in a pregnant patient with an umbilical hernia are presented in Table 19.3.

### Internal Umbilical Hernia Repair

The surgical technique consists of standard CS and umbilical hernia repair depending on the diameter of the umbilical defect. Anesthesia can be general or epidural/spinal. CS steps include skin disinfection with povidone-iodine, a Pfannenstiel skin incision in the lower crease, fetal delivery, and uterine wound closure, maintaining good hemostasis. Patients receive anti-



**Table 19.3** Surgical management of pregnant patients with an umbilical hernia

|                                                 | Suture repair                              | Mesh repair                                                       |                                                                    |
|-------------------------------------------------|--------------------------------------------|-------------------------------------------------------------------|--------------------------------------------------------------------|
| Umbilical hernia in woman planning a new baby   | High risk of recurrence                    | Pain in third trimester                                           | Repair is postponed until birth for small and asymptomatic hernias |
| Umbilical hernia diagnosed during pregnancy     | High risk of recurrence                    | Infection risk for pregnant woman especially in emergency repairs | Repair is postponed until birth for small and asymptomatic hernias |
| Cesarean section and simultaneous hernia repair | Easier                                     | Requires separate incision                                        | Patient satisfaction can be high                                   |
|                                                 | May be performed without separate incision | Lengthen operative time                                           | Patient's preference should be asked                               |
|                                                 | High risk of recurrence                    | Infection risk in puerperium                                      |                                                                    |
| Hernia repair after childbirth                  | No exact recommendation for timing         | No exact recommendation for timing                                | A 1-year interval may be recommended                               |
|                                                 |                                            |                                                                   | Repair can be postponed for another pregnancy                      |
| Concomitant diastasis recti                     | High risk of recurrence                    | Recommended                                                       | Patient should be informed about diastasis                         |

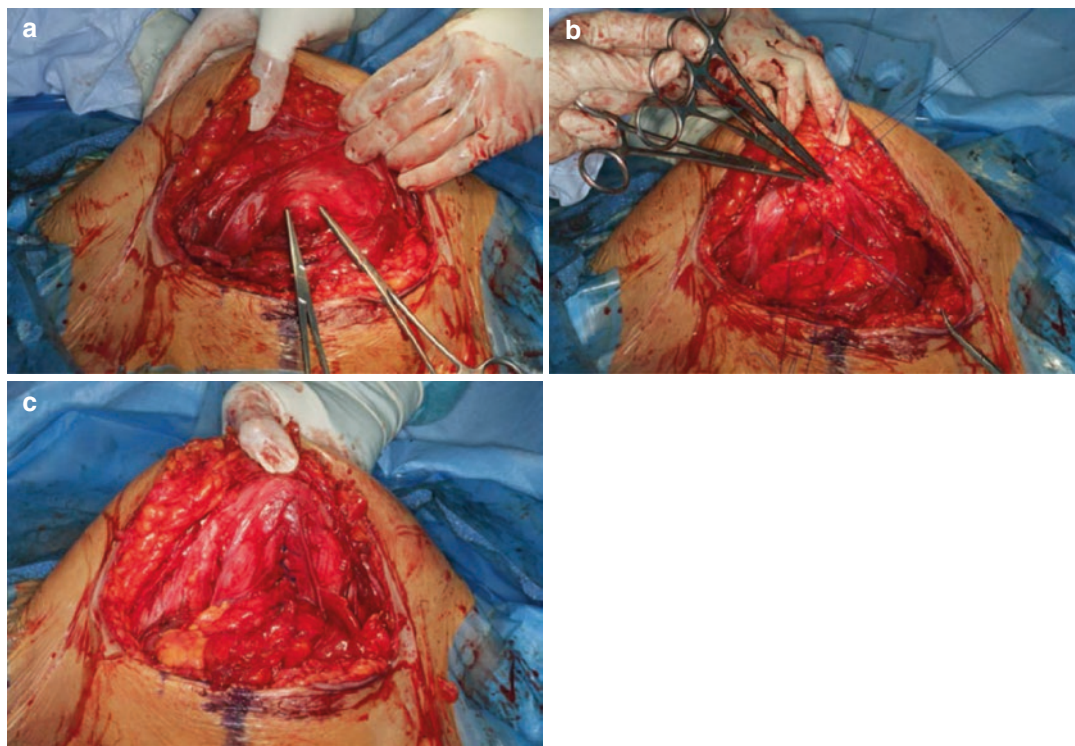
Reproduced with permission from [126] under the CC Attribution License

otic prophylaxis IV cefotaxime 1 g after placental extraction.

A Kocher clamp is placed in the middle of the rectus abdominis sheet at the edge of the upper abdominal flap for suture repair of the umbilical hernia. The flap is retracted superiorly to expose the peritoneal aspect of the umbilical defect. A vertical incision is made in the peritoneum underlying the umbilicus, and the caudal edge of the defect is identified by palpation. A second Kocher clamp is applied to this edge for traction and exposition of the defect. The assistant held the clamp in place, while the surgeon approximated the edges of the fascia with a continuous or interrupted 2-0 polypropylene suture, starting at least 1 cm caudal to the defect, and ending 1 cm cranial to the superior edge of the defect (or a total of 4 cm from the starting point). Due to higher collagen content, it is easy to palpate the caudal border of the umbilicus. In contrast, the cranial border is indistinctive due to the attenuated collagen structure and is not easily palpable. A partial wall defect may remain if the suture line is too short, resulting in a missed hernia even if the defect cannot be palpated. An approximation of a 4 cm part of the midline abdominal wall around the defect should be made. Subsequently, the peritoneum overlying the defect is closed with a running absorbable suture (Fig. 19.30), followed by standard closure of the CS abdominal wall incision [137].

Compared to CS, internal umbilical suture repair with CS prolonged operation by 20 min and hospitalization by 0.5 days. No differences in postoperative analgesia, loss in hemoglobin, postoperative complications, and wound infection rates were found [137]. The high recurrence rate of 28% (internal + external hernia repair) is comparable to recurrence rates in nonpregnant adults treated with direct suture repair [137]. Combined umbilical hernia suture repair and CS might be challenged by the high recurrence rate, giving the option for hernia repair with the mesh (Fig. 19.31). Moreover, it is unknown whether symptomatic umbilical hernias during pregnancy remain symptomatic after delivery.

There are no recommendations for simultaneous repairs, but mesh repair is recommended if an umbilical hernia is >3 cm [77]. One option is preperitoneal nonabsorbable mesh implantation. After CS, the patient is in Trendelenburg position to make the viscera away. The hernia contents are reduced from the inside of the abdominal cavity, and the hernia sac or pathological contents are excised. A peritoneal incision is placed around a defect in the posterior sheath (neck of hernia), and then, upper and lower peritoneal flaps are dissected. The hernial sac was pulled from inside and excised. If the umbilicus was distorted, it should be fixed with an absorbable 2-0 suture to the sheath. Closure of fascial defect is made with continuous absorbable suture size 1. Polypropylene



**Fig. 19.30** (a) Abdominal wall is lifted, and the fascia borders of the umbilical hernia defect are palpated and grasped with Kocher clamps. (b) Several interrupted polypropylene sutures are placed, closing the fascia longitudinally. (c) After knotting the sutures, the peritoneum is closed, thus covering the polypropylene sutures. (Reproduced with permission from [137])

mesh (6 × 11 cm) is fixed to the posterior aspect of the sheath by continuous and interrupted non-absorbable sutures 2-0, followed by the closure of peritoneal flaps over mesh without a drain. There were no differences in maternal outcome and recurrence rate compared to simultaneous umbilical hernia repair with separate incision and delayed umbilical hernia repair after healing CS scar [138].

After CS, umbilical hernia repair is performed by placing an intraperitoneal mesh covering the defect. The mesh is fixed with nonabsorbable sutures. Pfannenstiel's incision is closed in a standard fashion [77]. The rate of seroma or hematoma, wound infection, wound disruption, or loss of hemoglobin was the same as in the CS group [77]. In the same study, suture repair resulted in a recurrence of 2.8%, whereas no recurrence was detected in the mesh group.

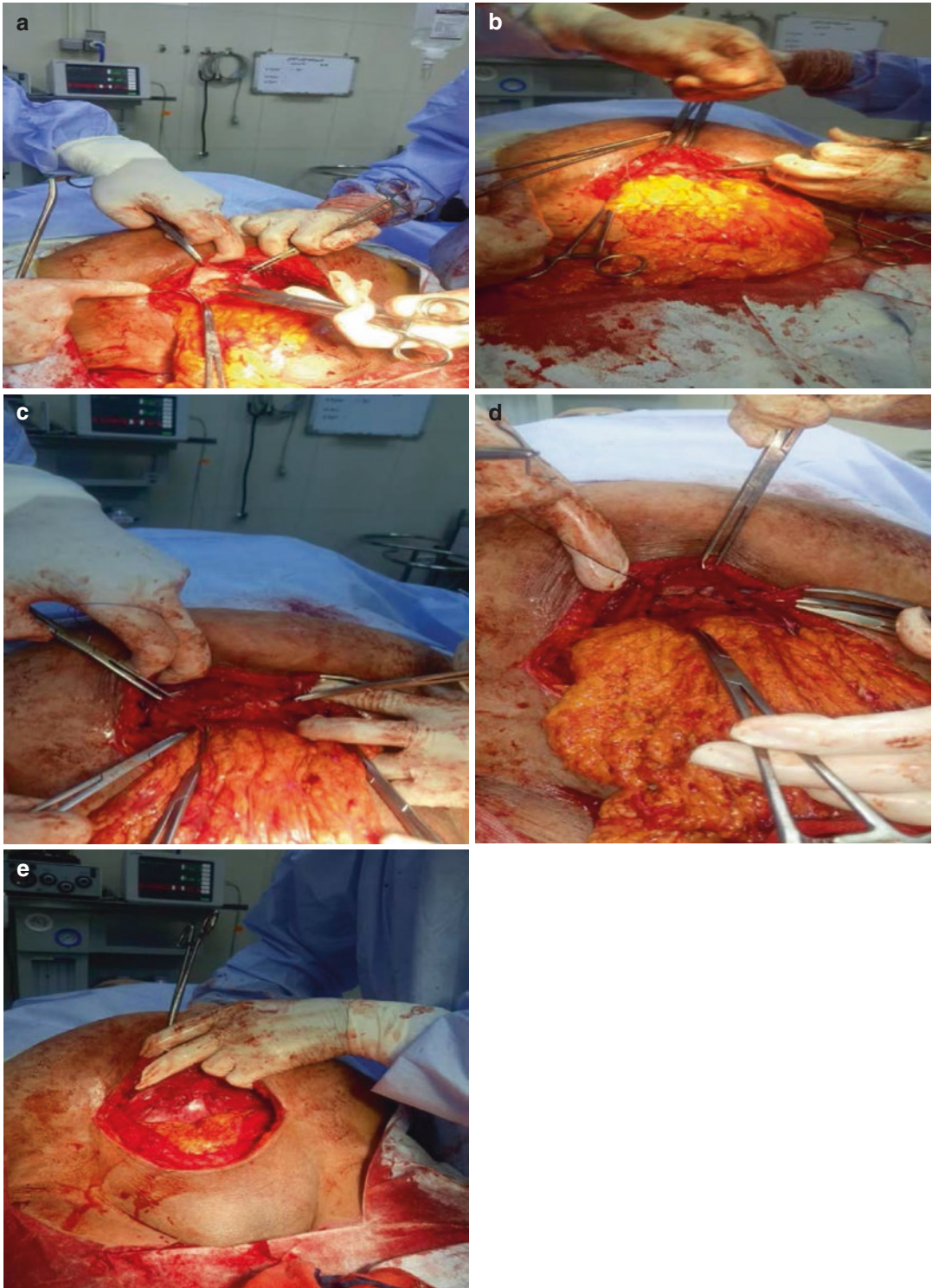
nally. (c) After knotting the sutures, the peritoneum is closed, thus covering the polypropylene sutures. (Reproduced with permission from [137])

### External Umbilical Hernia Repair

After the closure of the Pfannenstiel incision for the CS, a paraumbilical semilunar skin incision is performed. The hernia sack is dissected and opened, and the hernia contents are reduced. The fascia defect is closed either longitudinally or transversally using several interrupted sutures with nonabsorbable material 1-0. Subcutis and skin were closed in a standard fashion [137]. If mesh insertion is indicated, it is more convenient to use internal umbilical hernia repair.

#### 19.2.7.3 Uterine Fibroids in Umbilical Hernia

Most uterine fibroids in pregnancy are asymptomatic [128]. No treatment is needed for intramural and subserosal fibroids of ≤3 cm. Only 10% of previously diagnosed fibroids



**Fig. 19.31** Operative steps of paraumbilical hernioplasty during the Cesarean section. (a) Elevation of peritoneal flaps from the posterior sheath; (b) reduction in the hernia content; (c) closure of posterior sheath by continuous

sutures; (d) fixation of the mesh over the sheath; (e) closure of peritoneum over the mesh. (Reproduced with permission from [138] under the CC BY 4.0)

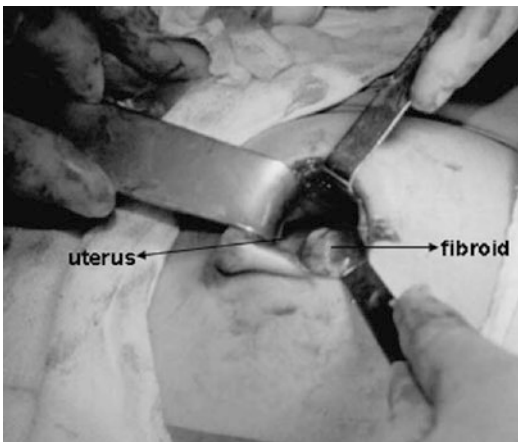


cause complications during pregnancy or delivery. Although some complications are due to changes in the anatomical localization of the fibroids during pregnancy, the most common complication is pain due to degeneration [128]. The first report of incarcerated umbilical hernia with a fibroid during pregnancy was by Ehigiegba and Selo-Ojeme in 1999 [128]. As a rule, fibroids without bleeding, hematoma, necrosis, or rupture are not resected. They are gently pushed into the abdominal cavity (Fig. 19.32), and the umbilical hernia is repaired [121]. With symptomatic myomas, myomectomy is followed by hernioplasty [128]. If the fibroids are not resected, the obstetrical US on the first postoperative day evaluates uterine fibroids, the uterus, and fetal status [139].

#### 19.2.7.4 Gravid Uterus in Umbilical Hernia

*When the patient stood upright, the fundus of the uterus was at a lower level than the symphysis pubis. Per vaginam, the cervix could not be reached. The uterus was thus almost completely upside down, and it was acting as a lever with the lower edge of the hernial orifice as the fulcrum.*

(Thomson SW, 1962)



**Fig. 19.32** The edematous, subserosal sessile fibroid without signs of bleeding, hematoma, or necrosis seen from the umbilical incision, which was not resected. (Reproduced with permission from [121])

#### Historical Remarks

Sylvester Saxtorph (see Sect. 24.1.1) recorded a case of a woman with four previous normal labors. The gravid uterus escaped through the abdominal wall and hung down below the knees, but it was observed that a very thick, broad pedicle projection passed up through it into the abdomen. She went on to term when the uterus became the site of violent contractions, sending the fetus up through the abdominal portal and down, out and alive through the natural passages. He followed up the contracting uterus, pressed it inside, and there it remained. The point of the emergence of the hernia was not a normal canal but an opening through the muscles [140]. Typyakov, in 1895, reported the first published case of the strangulated uterus in a subumbilical hernia. It was a 23-year-old woman, five-month pregnant [141]. She developed severe abdominal pain, which suggested that abortion was likely. The hernial ring was incised, the uterus was replaced in the abdomen, and the hernia was repaired. The patient recovered and had a term delivery.

#### Incidence

Incidence of the gravid uterus in anterior abdominal wall hernia varies. In Nigeria, before 1975, it was 1/12,439 deliveries [142]; in Zambia, in 1965, it was 1/5032 deliveries [143]. The presence of a gravid uterus in the sac of an umbilical hernia is extremely rare. This is because by the time the gravid uterus reaches the level of the hernial orifice, it is usually too large to enter the sac.

#### Diagnosis

Diagnosis is clinical. The uterus with fetal parts can be palpated through the thinned skin of a large umbilical hernia (Fig. 19.33). Auscultation of fetal sounds within the hernia confirms the diagnosis.

#### Treatment

Conservative surgical treatment follows the indications for incisional hernia (see Sect. 19.4.5). It has been suggested that the laxity of the abdominal wall and the presence of an enlarged, hypertrophied uterus could weaken a repair. Despite

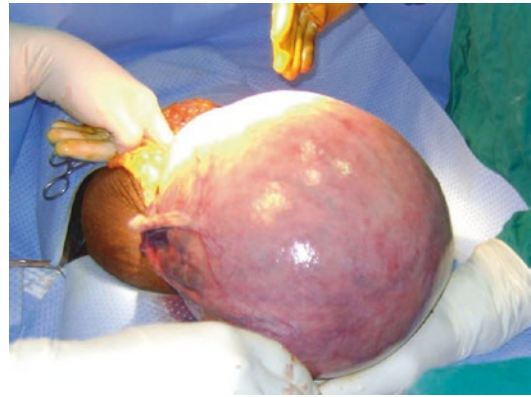


**Fig. 19.33** Blanket around the abdomen shows the lower limit of the hernia neck. Fundal height can be gauged from that of the hand. (Reproduced with permission from [90])

these theoretical concerns, different types and locations of hernias have been successfully operated as part of the CS (Fig. 19.34). There is no increase in wound infection rates or recurrences.

An umbilical hernia containing a gravid uterus should be repaired after CS during the same operation. It eliminates potential bowel obstruction between pregnancies or gravid uterus incarceration in subsequent pregnancies.

Indications for mesh placement are the same as in the nonpregnant population, although



**Fig. 19.34** Full-term pregnancy in an umbilical hernia. A cesarean section was followed by suture hernia repair (mesh was not available). The repair was intact at follow-up >1 year after surgery; the baby was healthy and developing normally. (Reproduced with permission from [96] under the CC BY 2.0)

suture repair was common [143]. The suture repair of a large defect may result in tissue tension associated with high recurrence. Uterine strangulation or fetal distress [143] are indications of emergent operation. With intrauterine growth retardation, uterine incarceration in a hernia should be excluded. Thomson described another indication for CS when the upside-down position of the uterus in a giant umbilical hernia prevents normal vaginal delivery: “*When the patient stood upright, the fundus of the uterus was at a lower level than the symphysis pubis. Per vaginam, the cervix could not be reached. The uterus was thus almost completely upside down, and it was acting as a lever with the lower edge of the hernial orifice as the fulcrum*” [90]. Several ruptured umbilical hernias resulted in the so-called *burst abdomen* (see Chap. 3). Cases of vaginal delivery followed by delayed hernia repair were described [144].

#### 19.2.7.5 Obstetric Management

Multiple complications have been reported associated with pregnancies in anterior abdominal wall defects. These include miscarriage, premature labor, intrauterine hemorrhage, intrauterine growth retardation, intrauterine death, rupture of the lower uterine segment, and death [97, 145]. Rupture of the lower uter-



ine segment and the delivery through the posterior fornix (colporrhexis) have also occurred [146]. This happens when labor is allowed to continue with the hernia unreduced. In such cases, the force of the uterine contraction is directed backward toward the sacrum instead of downward and forward toward the vagina [142].

## 19.2.8 Prognosis

### 19.2.8.1 Maternal Outcome

The suture repair of a large defect may result in tissue tension associated with high recurrence. In addition, such repair may cause raised intra-abdominal pressure, which is additionally exaggerated in advanced pregnancy, increasing the possibility of abdominal wall suture rupture. Maternal respiratory complications, including atelectasis and pneumonia, could be prevented or minimized by (1) hernia repair without tension, mostly with mesh repair, and (2) chest physiotherapy and early ambulation. One of the first published cases of strangulated large umbilical hernia by Coley and Hogue in 1918 resulted in wound infection and recurrence 8 months postoperatively [86].

### 19.2.8.2 Fetal Outcome

The American College of Surgeons National Surgical Quality Improvement Program revealed 126 pregnant women with umbilical hernioplasty in 10 years. Incarceration or strangulation existed in 50%. There was no fetal loss, even in cases of emergencies [133]. Premature delivery with the gravid uterus in an umbilical hernia is common.

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## 19.3 Epigastric Hernia

### 19.3.1 Historical Perspective

Charles E. Boys published the first case of a supraumbilical hernia in 1945. Manual reduction in incarcerated hernia at term failed, and emergency CS was performed [147].

### 19.3.2 Incidence

An epigastric hernia is in the midline on the anterior abdominal wall, between the umbilicus and the xiphoid, and through a defect in the linea alba. It accounts for 1% of all hernias in the general population. However, the true incidence may be higher because most are asymptomatic, and many patients do not seek medical advice. There are two reports during pregnancy with three patients [127, 132].

### 19.3.3 Clinical Presentation

There can be a history of reducible epigastric swelling. Swelling can be painless but can become painful and even irreducible over time. Obstructive bowel symptoms should be checked. Temperature and hemodynamic stability should be checked before an obstetrical examination.

### 19.3.4 Differential Diagnosis

Differential diagnosis is almost identical to an umbilical hernia (see Sect. 19.2.5). Expansive intra-abdominal pathology, such as large uterine fibroids in advanced pregnancy, should be excluded.

### 19.3.5 Diagnosis

The diagnosis of an epigastric hernia, reducible or incarcerated, is almost always clinical. Hernias are mostly small, located from 2 to 10 cm above the umbilicus in the midline. The US confirms the diagnosis (see Sect. 19.2.6.2). With incarceration, vaginal examination is usually normal initially [147].

### 19.3.6 Treatment

#### 19.3.6.1 Indications and Timing

Depending on the presentation, a proposed management algorithm for epigastric hernias in preg-

nancy (Fig. 19.35) is watchful waiting or emergency herniorrhaphy. In advanced pregnancy, the uterus covers the defect minimizing the possibility of incarceration. For timing, see Sect. 19.2.7.1.

### 19.3.6.2 Surgical Techniques

Emergently operated epigastric hernias during pregnancy can be treated by an open or laparoscopic approach. Epigastric hernias are usually small with bulging of the preperitoneal fat. Therefore, an open approach with a small incision is the method of choice. Laparoscopic repair is preferred for large or concomitant abdominal wall hernias [148]. The disadvantage of laparoscopic repair is the use of mesh, which should sometimes, depending on the location, be transected if CS is indicated later. Such situations carry a higher risk of hernia recurrence.

### 19.3.7 Prognosis

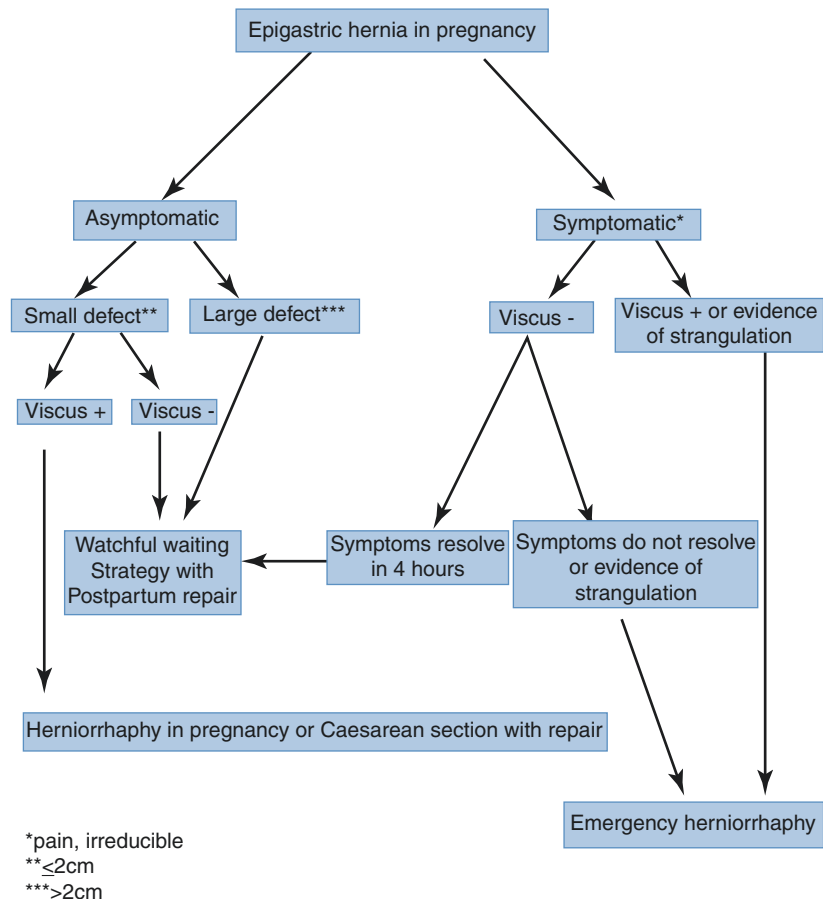
The prognosis is excellent due to the apparent clinical diagnosis and extremely rare incidence of incarceration in the general and pregnant population [127, 132].

## 19.4 Incisional Hernia

### 19.4.1 Historical Perspective

Karl von Bardeleben demonstrated before a convention in Berlin in December 1911 a case of pregnancy occurring soon after a pelvic laparotomy where the operative wound had broken down. This was followed by an IH. At presentation, the gestation was in the eighth month, and healed abdominal walls were “thin as paper.” The author advised waiting until term; then, a CS

**Fig. 19.35** Management algorithm for epigastric hernias in pregnancy. (Reproduced with permission from [127])



should be performed if difficulty presented during a spontaneous delivery. There was no report on the outcome [149].

### 19.4.2 Incidence and Risk Factors

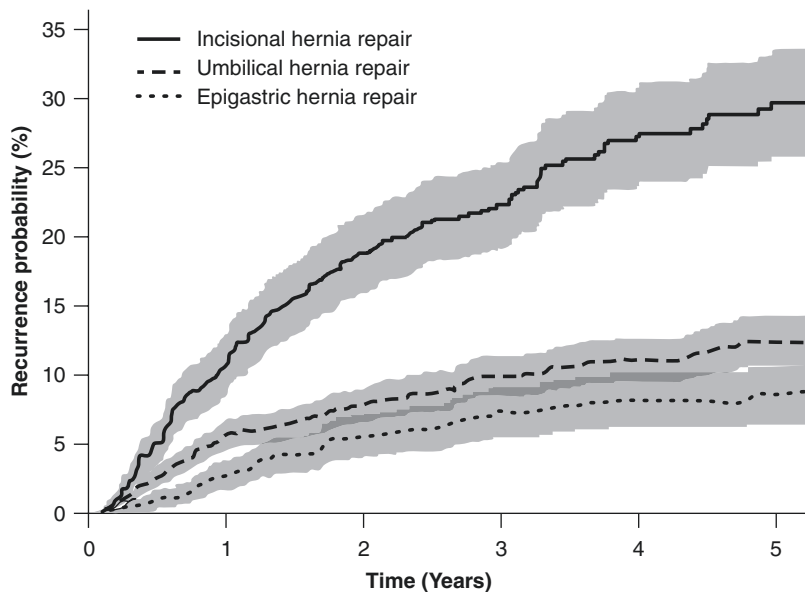
The incidence of an incisional (IH) or a postoperative hernia in the general population is up to 18.7% at 10 years [128]. It must be differentiated from early wound dehiscence with evisceration with 1–3% of laparotomies that require immediate reoperation [128]. The incidence of a postoperative hernia is 3% following CS due to defective abdominal wound healing and herniation of the gravid uterus through the abdominal wall [128]. It is associated with midline incisions, the need for additional operative procedures, longer administration of antibiotics and more potent antibiotics, postoperative abdominal distension, intra-abdominal sepsis, residual intra-abdominal abscess, wound infection, wound dehiscence, and postoperative fever [128]. The incidence of a postoperative hernia in pregnancy is unknown. There are only case reports regarding this condition. There may be several reasons for the condition's estimated low incidence. First, pregnant patients represent a young and healthy population who have been operated on successfully in the earlier neonatal or childhood period or were

never operated on. Second, patients with IHs who plan future pregnancies probably subdue to operation before pregnancy.

A pregnancy following IH repair is associated with an almost twofold increased risk of recurrence. In contrast, there is no difference in the risk of chronic pain compared to women with and without a subsequent pregnancy [150]. Incisional and umbilical hernia repair has a higher risk of recurrence than epigastric hernia repair (Fig. 19.36).

Conservative management seems recommendable for women with no or little discomfort who plan a future pregnancy [151]. A suture repair might be better in symptomatic women who require a repair before pregnancy, postponing a mesh repair after the last pregnancy in case of hernia recurrence. Although suture repair carries double the risk of recurrence than mesh repair, it has a 5× lower incidence of chronic pain in a subsequent pregnancy [151]. Further, women who had given birth previously were at increased risk of recurrence than nulliparous women at index repair. This could be due to the increased prevalence of abdominal rectus diastasis in parous women associated with hernia recurrence

**Fig. 19.36** Five-year probability of hernia recurrence stratified on type of hernia with 95% confidence. (Reproduced with permission from [124])



[151]. There is no difference in the risk of recurrence after mesh versus suture repair in women without a subsequent pregnancy [151].

#### 19.4.2.1 Incisional Hernia with Gravid Uterus

Herniation of a gravid uterus through an IH of the anterior abdominal wall is rare because, by the time the uterus reaches the level of the hernial aperture, it is usually too large to enter the hernial sac [152]. Also, patients with large defects seek help because large IHs are primarily symptomatic before conception. Arthur Holmes, in 1906, published the first case [153]. Cartaya reported a case in which a uterus the size of a four and one-half months' pregnancy became strangulated in an IH [154]. Severe abdominal pain and vomiting ensued. Mechanical attempts at reduction failed, and operation was advised. The constricting ring was cut, the pregnant uterus returned to the abdominal cavity, and the hernia was repaired. The patient had normal-term delivery.

Less than 20 cases of IH complicated by pregnancy were published; approximately 50% developed incarceration with or without subsequent strangulation, commonly after 4 months of gestation [93, 147, 152, 155–165]. Infraumbilical vertical incisions performed for CS and wound infections are the most common risk factors [93, 152, 156, 166]. Unfortunately, most CS in some undeveloped/developing countries is performed by non-specialist general duty doctors who do not have additional obstetrics and gynecology training. In previous decades, the high frequency of wound failure in undeveloped countries was due to catgut repair of fascia, particularly when the wound is contaminated or infected [167]. Therefore, in contrast to infraumbilical midline incisions, transverse suprapubic incisions have very low rates of IH due to the orientation of the incision and the forces acting on it [166, 168].

#### 19.4.2.2 Incisional Hernia with Abdominal Wall Endometrioma

Abdominal wall endometriomas are divided into *spontaneous abdominal wall endometrioma* and *scar endometrioma*. Scar endometrioma results

from abdominal wall incisions, most commonly after gynecologic operations. The most common site for extrapelvic endometriosis is the Pfannenstiel incision scar, with an incidence of 0.03–1% [57, 169–171]. It is known as *cesarean scar endometriosis*. Studies from India showed a much higher proportion after hysterotomy for mid-term abortion than CS: 71–74% and 4–6%, respectively [172, 173]. In these countries, abortion via a hysterotomy was relatively common.

Early hysterotomy in pregnancy is the main risk factor for abdominal wall endometriosis.

#### 19.4.3 Clinical Presentation

Clinical presentation resembles incarcerated umbilical hernia (see Sect. 19.2.4). History (previous operations) and clinical examination (abdominal wall scars with a palpable defect in the abdominal wall and distension) are sufficient for the diagnosis. The diagnosis of a gravid uterus in an IH is made by the history of a hernia between pregnancies, an unusual bulge in the abdomen with stretched skin [93, 152], and easily palpable uterus and fetal parts [93, 160]. Types of complications at presentation resemble umbilical hernia in pregnancy:

- Incarcerated IH,
- Incarcerated gravid uterus in an IH,
- Skin ulceration/skin necrosis overlaying IH,
- An IH with spontaneous skin rupture at the point of skin necrosis.

Excessive skin stretching could result in skin ulcerations. Further progress causes skin necrosis and, finally, skin defects. With incarceration, the uterus becomes irreducible. Incarceration and strangulation present with severe abdominal pain and vomiting [147, 165].

### 19.4.3.1 Incisional Hernia with Gravid Uterus

A gravid uterus in an IH is confirmed by the history of a hernia between pregnancies, an unusual bulge in the abdomen with stretched skin [93, 152], and easily palpable uterus and fetal parts [93, 160]. In large hernias with a gravid uterus in advanced pregnancy, skin discoloration, excoriation, and ulceration could be present (Fig. 19.37). These skin changes are found at the apex of pendulous herniation due to skin ischemia and subcutaneous tissue. However, changes can be present on the entire skin over the herniated gravid uterus or around the previous incision [174, 177]. This results from skin stretching aided by acute angulation of arteries supplying

the tip of a hernia [175]. IH without a gravid uterus as a hernial content rarely causes skin necrosis and skin defect. In most cases, the gravid uterus is so large that there is no possibility of the evisceration of abdominal viscera. The final result of skin compression results in skin defect (Fig. 19.38).

Fetal lies and presentation sometimes could not be ascertained. Fetal position and palpation are not possible with polyhydramnios [163]. The reported incidence of incarceration is 53%, and the uterus is irreducible with or without any other symptoms. The strangulation results in fetal distress, severe abdominal pain, vomiting, or shock [175]. With incarceration, vaginal examination is usually normal initially.



**Fig. 19.37** Cesarean scar hernias in advanced pregnancy. Decubital skin ulcers develop in the lowest part of a hernia. (Reproduced with permission from [174–176] under the CC BY 3.0)





**Fig. 19.38** Incisional hernia at 26 weeks of pregnancy with a skin defect of 15 × 15 cm with surrounding skin ulcerations. (Reproduced with permission from [178])

#### 19.4.3.2 Incisional Hernia with Abdominal Wall Endometrioma

The classic symptoms of an abdominal wall endometrioma are cyclic or catamenial pain associated with a (painful) mass. However, cyclic pain is not a universal characteristic of pain [172, 179, 180], present in 57% of patients. However, a mass (96%) or pain (87%) is more common. Other common signs and symptoms are bleeding from superficial lesions and lower abdominal pain [170, 172, 173, 181].

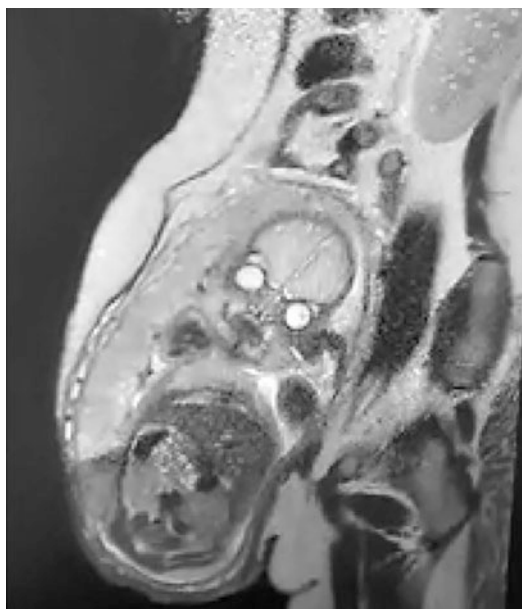
Physical examination should determine the fascial defect (hernia) and if the mass feels as if it were attached to the anterior fascia. No further studies are necessary for classic presentation [182]. The accurate preoperative diagnosis rate varies from 20 to 50% [62, 172]. One explanation of the diagnostic failure is that the diagnoses were made commonly by general surgeons not familiar with this entity.

### 19.4.4 Diagnosis

In doubtful cases, the transabdominal US defines a hernia and structures in the hernia sac. A rare but severe obstetric condition is gravid uterus herniation into an anterior abdominal wall through an IH [160, 161]. The transabdominal US confirms complications, including strangulation, abortion, premature labor, accidental hemorrhage, intrauterine death, and lower uterine segment rupture [161].

#### 19.4.4.1 Incisional Hernia with Gravid Uterus

Clinical diagnosis is straightforward (see Sect. 19.4.3.1). The transabdominal US and abdominal MRI (Fig. 19.39) confirm the diagnosis [160, 162], define a fetal position, and detect signs of fetal distress. Terminologically, fetal orientation in hernia could be wrong because of the relation between fetal position and cervix changes due to uterine fundal drop into the hernia sac (Fig. 19.39). The uterus is acutely anteverted [144].



**Fig. 19.39** Sagittal abdominal MRI of a “breech” presentation in the incisional hernia sac. (Reproduced with permission from [183])

#### 19.4.4.2 Incisional Hernia with Abdominal Wall Endometrioma

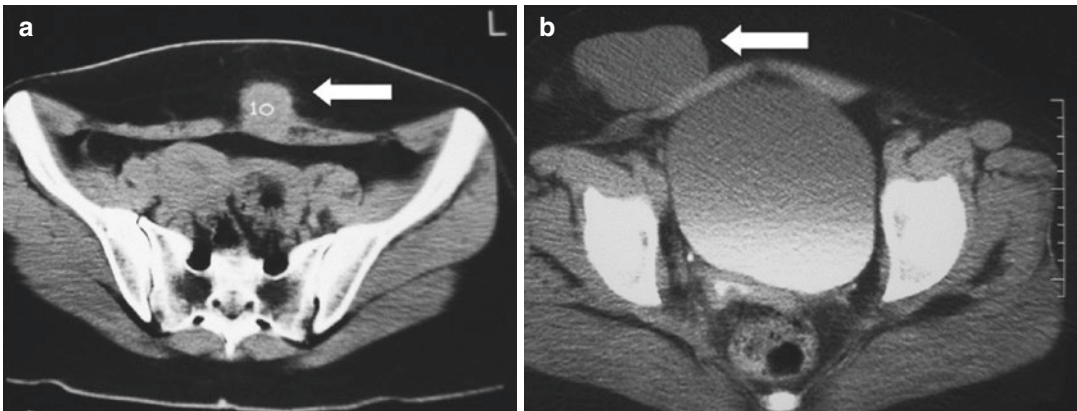
Physical examination with a classic presentation eliminates the need for further studies [182]. The US shows a hypoechoic and heterogeneous mass with scattered internal echoes (Fig. 19.11). Some masses appear completely solid, sometimes with cystic changes (see Sect. 19.2.5.2) [57]. Endometriosis has no pathognomonic CT findings, as appearances depend on the menstrual cycle phase, the proportions of stromal and glandular elements, the amount of bleeding, and the degree of surrounding inflammatory and fibrotic response (Fig. 19.40). Due to the relatively vascular nature of these lesions, enhancement often occurs on CT scans with IV contrast [185]. Due to its very high spatial resolution, MRI enables the detection of very small lesions and distinguishes the hemorrhagic signal of endometriotic lesions (Fig. 19.41) [187]. Imaging studies may be obtained if the lesion is very large, with a concern for fascial involvement or doubtful diagnosis. These data may assist with surgical planning if an abdominal wall reconstruction is anticipated.

### 19.4.5 Treatment

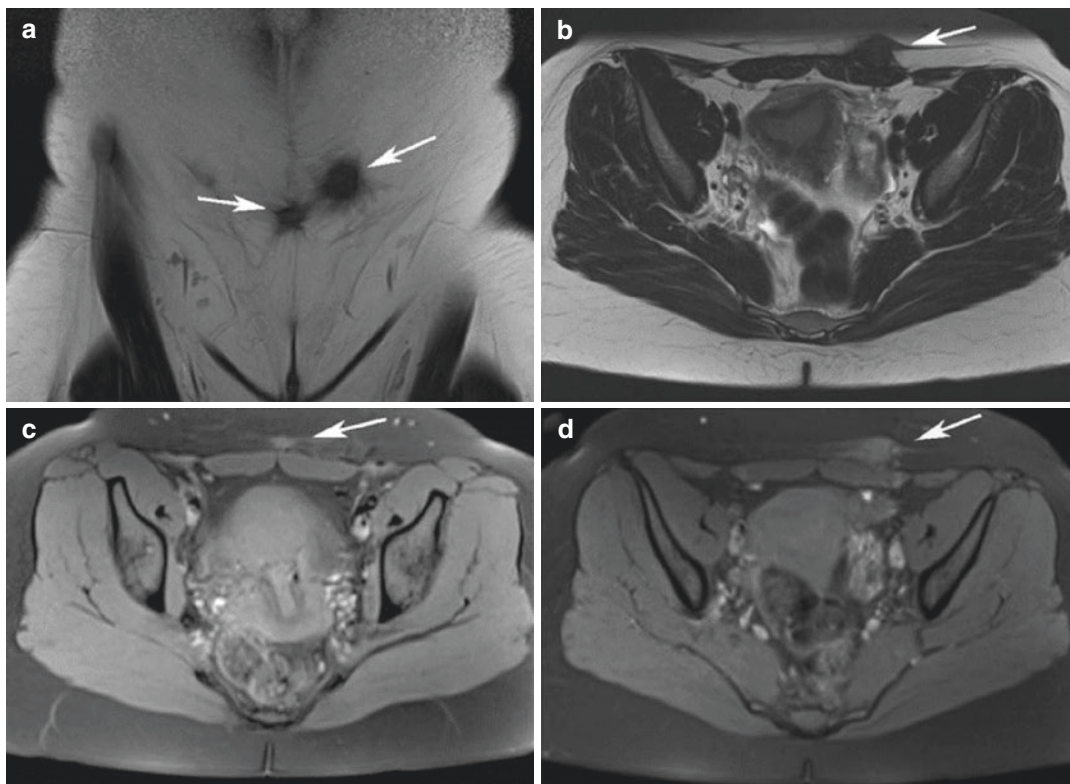
#### 19.4.5.1 Indications

In prepregnancy patients, if the hernia is large and symptomatic, it may be better to do an elective repair is recommended by postponing pregnancy for 1 or 2 years. If the hernia is small or minimally symptomatic, it may be better to hold the repair until after delivery or after the last pregnancy [188].

The management of an IH without incarceration in pregnancy is mainly conservative [93, 152] until planned elective CS at 37 weeks. The uncertainty about wound integrity of the anterior abdominal wall and uterus during vaginal birth after previous CS has led most obstetricians to favor an elective CS as the safest mode of delivery [93], with simultaneous IH repair (see Sect. 19.4.5.5). Elective repair is indicated after vaginal delivery (see Sect. 19.2.7.1). Incarceration of the uterus or other organs indicates the emergent



**Fig. 19.40** CT of masses in the anterior abdominal wall, (a) in a vertical, and (b) in a Pfannenstiel incision (arrows). (Reproduced with permission from [184])



**Fig. 19.41** Abdominal wall endometrioma with a previous history of Cesarean section. (a) Coronal T2-weighted image shows two lesions, in the left corner of the surgery scar and more centrally; (b) axial T2-weighted image

shows lesion ventrally from the rectus abdominis; (c, d) axial T1-weighted images show the slightly high intensity of AWE lesions compared with muscle. (Reproduced with permission from [186] under the CC Attribution License)

operation. Most patients with uterine incarcerations had BMI >40 kg/m<sup>2</sup> [189–191].

The obstetric indication is emergency CS due to fetal distress or preterm labor [192, 193]. With every presentation and indication for the operation, consultation with the patient is important because bilateral tubal ligation can be offered to (multiparous) patients who do not wish to undergo any more psychosocial trauma of pregnancy in such circumstances [176, 192–194]. Without the possibility of further pregnancies, hernia repair with mesh is indicated [192], as for umbilical or epigastric hernias [134].

#### 19.4.5.2 Open Repair

Despite advances in surgical techniques and materials, adequate fascial closure is mandatory. The best method is mass closure using wide bites with the sutures sufficiently close together to

comply with *Jenkin's rule*, which declares the need for four times the length of material as the length of the wound [195]. *Smead-Jones mass closure* is the closure of all the abdominal wall layers (except the skin) as one structure. The layered closure includes the separate closure of the individual components of the abdominal wall. It is associated with a significantly higher dehiscence rate than mass closure (3.81% vs. 0.76%) [196]. Surgical techniques with a mesh should be used if a hernia is large. For IH repair before a planned pregnancy, mesh closure is recommended. Prosthetic mesh tends to contract and harden and may seriously interfere with abdominal expansion in pregnancies. Hernia repair with an absorbable, synthetic mesh can be used, particularly when a large defect is present, but recurrent hernia is likely. Another option is the use of bioprosthetic mesh. These meshes have been

successfully used in contaminated and infected hernia repairs. However, the risk to the fetus when using a biological implant for hernia repair is unknown. Also, the cost of bioprosthetic mesh is high, and the effect of the increased biomechanical stress and strain of the gravid uterus on the abdominal wall–bioprosthetic interface is unpredictable [189].

The fascial laxity resulting from pregnancy facilitates the ability to primarily close with nonabsorbable sutures, even large fascial defects, without tension and prosthetic material [176, 190, 194]. In a nonpregnant patient, fascial defects of such size require mesh repair. For the abdominal wall characteristics during pregnancy, see Sect. 19.6.1.

Therefore, in the largest study with the open repair on 27 pregnant patients, Abrahamson and Gorman recommend that these hernias are probably best repaired by the *shoelace technique* [197]. Nonabsorbable sutures are preferred due to increasing intra-abdominal pressure and suture line tension during pregnancy.

#### 19.4.5.3 Component Separation Technique

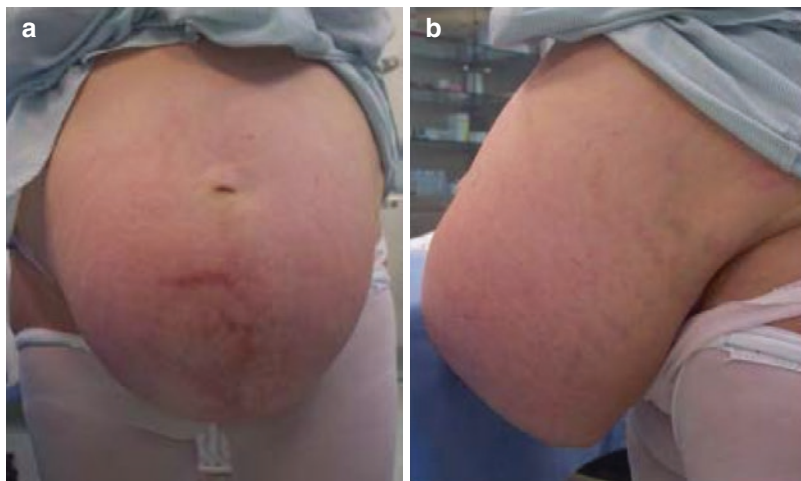
Since its initial description by Ramirez [198], the *component separation technique* has proven effective for treating giant abdominal hernias in which prosthetic material utilization is not indicated (Fig. 19.42). It can be used in emergency and elective settings. The first step in the standard

component separation technique is separating the skin and subcutaneous tissue from the anterior rectus sheath and external oblique aponeurosis. The latter is incised 2 cm lateral to the semilunar line to separate the external oblique from the internal oblique in their avascular plane, thus allowing the rectus abdominis complex to be brought medially and approximated with interrupted nonabsorbable sutures. Redundant skin is excised, and the incision is approximated over two closed suction drains. The postoperative course in the only published case was unremarkable, and the patient was discharged on postoperative day 5 with an abdominal binder during the first 4 weeks postoperatively [199]. Drains were removed on postoperative day 7. Follow-ups at 1, 6, and 12 months were without recurrence (Fig. 19.43). The role of the abdominal binder during the postoperative period after abdominal wall hernioplasty is not defined.

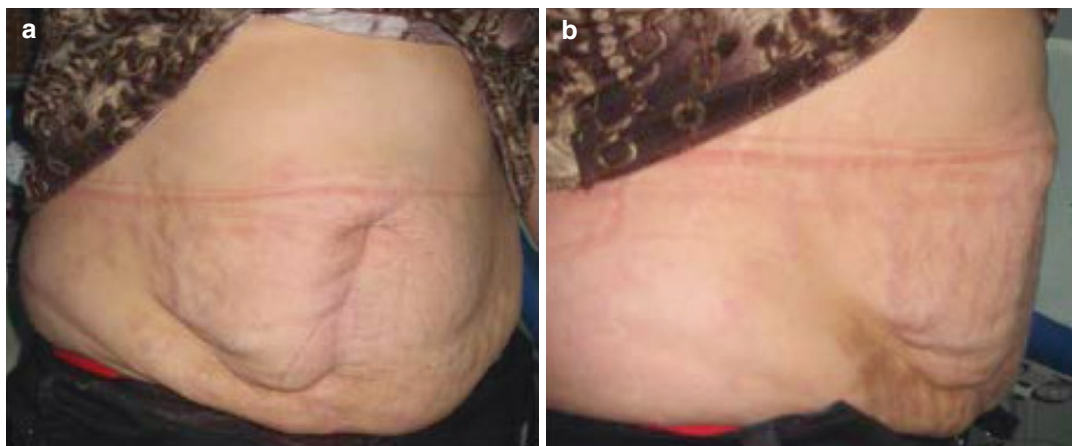
#### 19.4.5.4 Laparoscopic Repair

Data on treatment strategies for anterior abdominal wall hernias in women of childbearing age are scarce. No “best practice” guidelines exist. Data regarding laparoscopic repair are lacking. One case described laparoscopic hernia repair during pregnancy [148] and another was a successful vaginal delivery after a previous laparoscopic repair of an omphalocele [200]. Schoenmaeckers et al. described a unique series of eight women who got pregnant and gave birth

**Fig. 19.42** Preoperative (a) frontal view and (b) lateral view after four vaginal deliveries. An incisional hernia was secondary to an infraumbilical midline laparotomy and right oophorectomy for ovarian cystadenoma. (Reproduced with permission from [199])







**Fig. 19.43** Postoperative result after component separation technique. (a) frontal view and (b) lateral view. (Reproduced with permission from [199])

following laparoscopic repair of the ventral or an IH. Of those, four were IHs [132].

#### 19.4.5.5 Incisional Hernia with Gravid Uterus

##### Complications

Potential complications apart from uterine incarceration or strangulation include spontaneous abortion, preterm labor, accidental hemorrhage, postpartum hemorrhage, intrauterine growth retardation, intrauterine fetal death, and the complete evisceration of the gravid uterus [156], rupture of the lower uterine segment during labor [161, 163], or dysfunctional labor. Therefore, pregnant women and fetuses should be monitored closely, and any of these complications is an indication for intervention. With intrauterine growth retardation, the incarceration of the gravid uterus in IH is not the case when the uterus can be reduced easily [201].

Burst abdomen or skin rupture/defect during pregnancy is more frequent with an IH [164, 176, 178, 202] than other abdominal wall hernias.

##### Treatment

Managing a pregnant patient with a large IH with the gravid uterus in a hernia depends on the gestation period and obstetric emergency. As the uterus remains a pelvic organ in the first trimester, there is no risk of incarceration during this

period. In the second trimester, the pregnant uterus grows out of the pelvis, increasing the risk of incarceration.

Conservative management is efficient in a symptomless patient, with CS indicated at term [177]. Conservative methods with variable success include manual reduction in hernia contents, rest, abdominal binders, a daily wound dressing with emollients, antiseptics, or topical antibiotics for skin ulcerations [143, 147, 152, 164, 193, 203]. A fetus is monitored with daily fetal movement counts, weekly CTG, and an abdominal and fetal US every 3 weeks. Conservative treatment aims at a vaginal birth, providing time for healing and delayed repair [90, 167]. Spontaneous vaginal delivery should be tried if the pelvic contraction is excluded, particularly if the uterus can be maintained in a near-normal anatomical position [90, 143]. Vaginal delivery can proceed by correcting the acute uterine anteversion [144].

**Elective operation** during pregnancy is indicated when (1) despite conservative management, the uterus remains inside the large hernia sac with an increased risk of incarceration and (2) necrosis or ulceration of the overlying skin occur without evisceration.



No consensus exists regarding the timing of the surgical repair or optimal technique. Immediate and delayed repairs are used, with direct fascial closure or mesh repair [93, 156, 161, 163]. Antenatal repair of an IH containing a strangulated uterus early in the pregnancy, followed by normal completion of gestation at term, is described [165]. Some recommend simultaneous CS followed by hernioplasty [160, 177], especially with decubital skin ulcers (Fig. 19.34), which should be excised. Others claim that an IH during pregnancy does not indicate CS [163]. Sometimes lower segment CS may not be feasible due to the unusual shape and contour of the uterus and an unapproachable lower segment. In these conditions, a classic approach may be easier [147].

**Emergent operation** during pregnancy is indicated when herniation of the gravid uterus leads to incarceration, strangulation, burst abdomen, preterm labor, intrauterine growth retardation, accidental hemorrhage, intrauterine death, and rupture of the lower uterine segment [152, 164, 174]. CS is recommended if fetal maturity is reached.

The management of emergent conditions depends on the gestational age. Strangulation of the uterus at or near term requires emergent CS, followed by immediate hernia repair [204]. If the uterus is strangulated in early pregnancy, immediate repair is followed by pregnancy with a viable fetus taken to term. Care must be taken to avoid injuries to vital structures while entering the abdomen, such as the small or large bowel, as it can be contained in the hernial sac, and the skin and peritoneum covering it may be very thin [163]. Additionally, the enlarged uterus may make herniorrhaphy difficult and unsustainable. The nonabsorbable mesh should be routinely placed across an IH [174], although there are cases of suture repair [177]. Herniorrhaphy techniques are not standardized for this condition. In most case reports, the type of hernioplasty, the

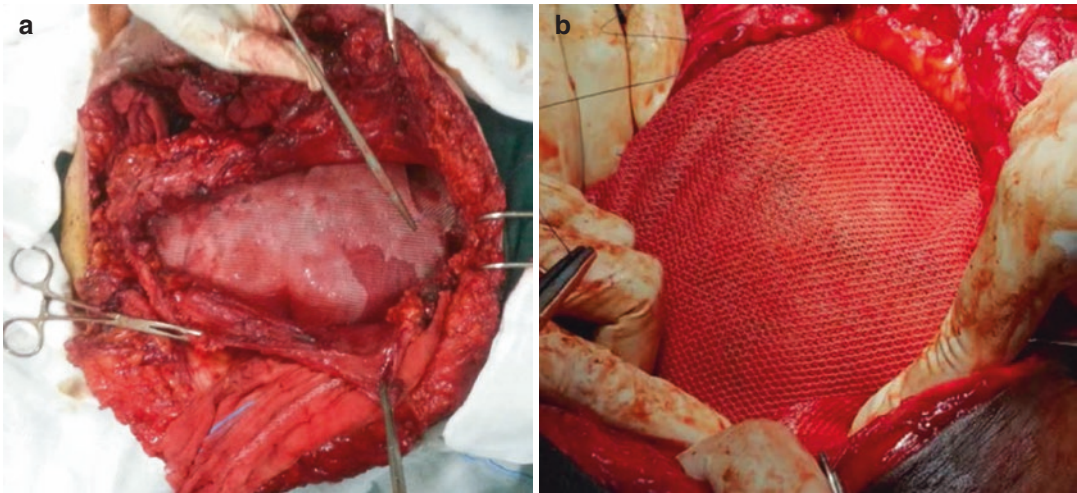
location of the mesh, or the type of mesh is not precisely described [203]. The mesh is sutured to the edges of the fascia (Fig. 19.44a) or placed retromuscularly (Fig. 19.44b). Long-term follow-up is unknown. Although some found that a mesh repair resulted in more complications and recurrences [79], others did not find an increased incidence of complications [183]. Potentially increased complications after mesh repair could be due to larger and more complex hernias repaired with the mesh.

Ulcerated and redundant skin should be removed, the hernia sac excised, and the uterus returned to the abdominal cavity. The orientation and extension of skin excision are not defined. Due to the redundant skin infraumbilically after post-CS incisional hernia, extended Pfannenstiel skin excision is used (Fig. 19.45). With a large hernia or hernia with supraumbilical extension, the best access is the incision over the scar from the previous operation, with an excision of ulcerated/necrotic skin. A subcutaneous suction drain is recommended [183]. Perioperative antibiotic prophylaxis is mandatory. Cosmetic effects are challenging to evaluate due to the different directions of incisions, their length, an extension of excised skin changes, and the location of mesh placement. Extended Pfannenstiel incision, especially over standard Pfannenstiel incision (Fig. 19.45), results in better cosmesis than other incisions (Fig. 19.43).

The role of the abdominal binder during the postoperative period in pregnancy and puerperium is unknown, although commonly used [183, 203, 205].

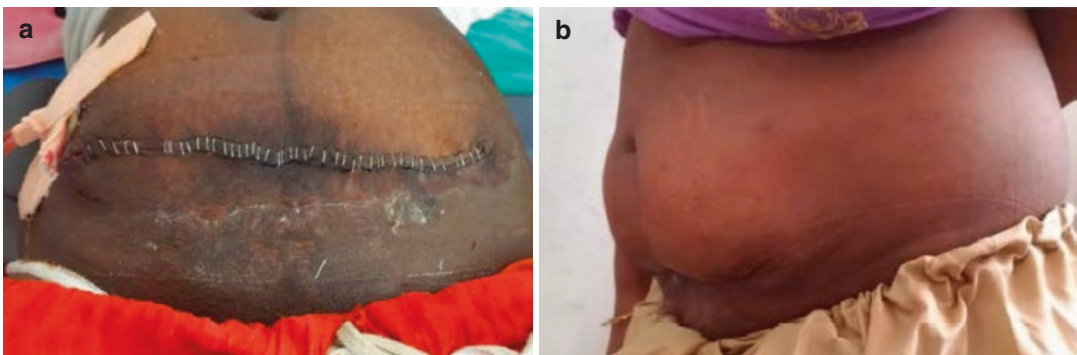
#### 19.4.5.6 Incisional Hernia with Abdominal Wall Endometrioma

Medical management often results in a temporary relief with the return of symptoms after the medication is discontinued. In addition, medications used during pregnancy could have harmful effects. The treatment of choice is wide local excision with negative margins [57, 206]. With at least a 1 cm margin, wide excision is considered the treatment of choice, even for recurrent lesions [179]. Abdominal wall endometrioma incorpo-



**Fig. 19.44** Simultaneous incisional hernia repair after cesarean section. **(a)** Reinforcement of the defect using a mesh sutured to aponeurosis. (Reproduced with permis-

sion from [203]). **(b)** Retromuscular placement of nonabsorbable mesh. (Reproduced with permission from [183])



**Fig. 19.45** **(a)** Early postoperative wound after cesarean section, necrotic skin excision, and mesh hernia repair of a gravid uterus in incisional hernia from previous cesarean

section. **(b)** Scar 2 months postoperatively. (Reproduced with permission from [183])

rated into the musculature requires en bloc resection of the underlying myofascial elements. Surgeons should be prepared for a coexisting hernia, and patients should be counseled that mesh repair may be necessary. Abdominoplasty and reconstruction with or without polypropylene mesh should be considered when a defect, even without a hernia in the abdominal wall, caused by wide excision occurs [207]. Procedures may be performed with local anesthesia, but unexpected surgical findings may change a plan, and general

anesthesia may be needed. Thus, these procedures should be performed in the hospital operating room. All biopsy tracts should be excised [179, 208]. No data in the general population support postoperative hormonal therapy. However, this may be appropriate in patients with a history of pelvic endometriosis [209] or recurrent cases when a combination of surgical re-excision with hormonal therapy is also recommended [210]. No recommendations exist for combined therapy in the pregnant population.

## 19.4.6 Prognosis

### 19.4.6.1 Prepregnancy Open Repair

With prepregnancy open repair on 27 patients, Abrahamson and Gorman recommend the *shoelace technique* [197].

General anesthesia is recommended. The old scar should be excised. The sac of a hernia and the rectus sheaths on each side are exposed. The new linea alba is constructed by suturing two vertical strips 1–1.5 cm wide, each split of the medial edge of each anterior rectus sheath, using a continuous over-and-over suture of a monofilament polyamide loop. This suture line returns the unopened sac and contents to the abdominal cavity. It approximates the edges of the anterior rectus sheaths by bringing them together at the new linea alba. A gap of varying width remains in larger hernias, with the continuous pliable to and fro shoelace suture adjusting itself to the differing widths and tensions across the fascial defect. The operation is entirely extraperitoneal and involves only two simple suture lines placed in normal healthy tissue; consequently, the postoperative recovery is smooth and rapid. In the usual Shoelace repair where the patient has passed the childbearing age, the second suture, the shoelace, is pulled tight under some tension to draw the flat muscles forward toward the midline. However, when young women intend to have further children, allowance must be made for the future distension of the abdominal wall with pregnancy by leaving the shoelace suture loose, with no tension. This requires a much longer length of suture material, which creates a good ratio between wound length and length of suture, making abdominal distension possible with no hernia recurrence after pregnancies [195, 211]. The monofilament nonabsorbable synthetic polyamide suture is strong, smooth, pliable, and inert and excites minimal tissue reaction. These characteristics allow the suture to slide easily through the tissues and adjust to the changing tensions and the lengthening of the repair as the pregnancy progresses. Furthermore, the polyamide suture has the added advantage of excellent extensile strength, which confers on the material the ability to “give” or stretch with the changing tensions on

the tissues and is, therefore, most suitable for shoelace repair in young women who plan future pregnancies.

Although authors did not observe recurrences during or after subsequent pregnancies or complications during pregnancies and deliveries, reservations regarding suture repair of even small hernias have higher long-term recurrence rates [212].

### 19.4.6.2 Prepregnancy Mesh Repair

The foreign body reaction and scarring associated with intraperitoneal mesh placement have, in theory, the potential to affect fertility and pregnancy. Given the expansion of the abdominal wall during pregnancy, biomaterial characteristics of shrinkage (>20%) and compliance should be considered. Large mesh implants may restrict abdominal wall flexibility [131, 213]. However, no data indicate that mesh repair of symptomatic ventral hernias should be prohibited in the reproductive woman who desires future pregnancy. A higher recurrence rate after mesh repair could result from larger and more complex hernias being repaired. There is a high rate (63%) of “tearing” or “pulling” pain at the area of the previous repair during the last months of pregnancy, with an intensity of  $\geq 50$  on a visual analog scale (scale 0–100) [132]. This pain disappeared immediately after delivery in all patients. All six women who had given birth before and after LRVIH mentioned more pain in the abdominal wall during pregnancy after LRVIH than before LRVIH. No chronic pain was experienced.

Pregnancy after mesh repair is limited to case reports [200, 214, 215] and case series [132], indicating that pain could be associated with mesh repair. This pain might occasionally require prolonged narcotic medications [214] or even IV “Patient-Controlled Analgesia” [215]. The observation that more pain is present during pregnancy after LRVIH than at pregnancy before LRVIH confirms the role of hernia repair in the genesis of this type of pain [132]. The pain after LRVIH might be caused by the mesh fixation [216] and the subsequent tension on this fixation during pregnancy. In a single small series, the technique of mesh fixation (either double crown tack

fixation or tacks and suture fixation) at LRVIH did not influence pain during pregnancy [132].

#### 19.4.6.3 Gravid Uterus in an Incisional Hernia

Premature delivery is common with vaginal delivery and emergent CS [167]. Rupture of the lower uterine segment and delivery through the posterior fornix (colporrhexis) are possible. This happens when labor is allowed to continue with the hernia unreduced. In such cases, the force of the uterine contraction is directed backward toward the sacrum instead of downward and forward toward the vagina. Also, due to a similar mechanism, uterine cesarean scar rupture/dehiscence can occur [183].

#### 19.4.6.4 Abdominal Wall Endometrioma

The recurrence rate in the general population is 4.3% [62]. Therefore, adequate surgical excision is essential to obtain a good outcome. No studies have addressed whether the surgical margin size affects the recurrence rate. The follow-up is inconsistent.

## 19.5 Parastomal Hernia

### 19.5.1 Classification

#### 19.5.1.1 Definition and Classification

A parastomal hernia is an IH related to an abdominal wall stoma [217].

Devlin classified parastomal hernias into four subtypes [218]:

- *Interstitial*, where the hernia sac lies within the layers of the abdominal wall,
- *Subcutaneous*, where the sac of a hernia lies in the subcutaneous plane,
- *Intrastomal*, where the sac penetrates a spout ileostomy,
- *Peristomal (prolapse)*, where the sac is within a prolapsing stoma.

No data are available to show differing complication rates or increased incidence of symptoms attributable to these different subtypes of a hernia. However, the classification system is helpful for comparison between different types of repair based on the subtype of a hernia. It also allows a specific description of any hernia detected by CT.

#### 19.5.1.2 Ostomy Types

Ostomies commonly seen in pregnant women include ileostomy, urostomy, and colostomy. An *ileostomy* is the most frequent. An ileostomy is the surgical creation of an opening into the ileum on the abdominal wall for fecal diversion. The principal indication for ileostomy in the younger population, including pregnant patients, is alimentary diversion due to ulcerative colitis and Crohn's disease. Increasing the volume of the uterus must be considered to prevent oppression of the stoma by the enlarged uterus with the subsequent onset of ileus. Therefore, it is appropriate to perform a stoma more cranially than standard (Fig. 19.46). A *colostomy* is the least frequently performed for fecal diversion in young adults. *Urostomy* (ureterostomy), or urinary diversion, is an opening created in the abdominal wall that allows urine to pass directly out of the body. It is indicated when long-term urine drainage through the bladder and urethra is not possible (e.g., after extensive surgery or in the case of obstruction). A fecal or urinary diversion in women of childbearing age is related to inflammatory bowel disease, neoplasm, congenital anomalies, trauma, malignancy, and polyposis syndromes [220]. The stoma may be on the abdomen over the right, transverse, or left side. Some paracolostomy herniation is almost inevitable, but complications are few, and normal pregnancy, delivery, and postpartum are expected [221].

#### 19.5.2 Incidence

A parastomal hernia is an IH related to an abdominal wall stoma. A parastomal hernia affects 1.8–28.3% of end ileostomies and up to 6.2% of loop





**Fig. 19.46** Normally functioning ileostomy in late pregnancy. (Reproduced with permission from [219])

ileostomies in the general population. Following colostomy formation, the rates are 4.0–48.1% and 0.3–31%, respectively [222]. Direct tissue repair or stoma relocation has recurrence rates of up to 50%, although the use of mesh lowers this considerably to 0–25% [223]. However, mesh placed in an onlay position around the stoma as a circumferential onlay can cause erosions or fistula formation in up to 5% of patients [224]. The prophylactic use of mesh prevents parastomal hernia formation by placing a lightweight sublay mesh during stoma formation [225]. A possible explanation for the extremely rare incidence of incarcerated parastomal hernias in pregnancy is due to the following:

- Elective closure before planned conception,
- Pregnancy as the relatively short period for the development of (clinically evident) a parastomal hernia,
- Decreased possibility of incarceration due to the protective effect of the enlarging uterus.

The incidence in pregnancy is unknown, but due to the increasing incidence of inflammatory

bowel disease, more and more pregnant patients with stomas would probably be present and therefore increased incidence of (incarcerated) parastomal hernias.

### 19.5.3 Clinical Presentation

#### 19.5.3.1 Medical History

No case reports are dealing with incarcerated parastomal hernias in pregnancy. The presentation of a parastomal hernia with small or large bowel, especially incarcerated, is more complex in the pregnant population because nausea and vomiting affect up to 80% of normal pregnant women in developed countries [221]. Constipation is common in the third trimester but may indicate a bowel obstruction in the pregnant ostomy patient. Intestinal obstruction is more likely to occur in mid- to late pregnancy when the fetal head descends and immediately postpartum when there is an acute change in the uterus size [221].

#### 19.5.3.2 Physical Examination

The examination involves removing the appliance and inspecting the surrounding skin. The examination should be performed in a standing and supine position, performing a Valsalva



maneuver [226]. A hernia appears as a bulge around the stoma. Digital examination of the stoma enables fascial aperture and parastomal tissue assessment.

Normally functioning stomas before pregnancy can enlarge and be at least 20 mm bigger (double) than before pregnancy.

This is a common situation, not a sign of ileostomy obstruction or (incarcerated) a parastomal hernia. Asymptomatic patients with normally functioning stomas can be reassured, and diagnostic workup is unnecessary.

#### 19.5.4 Diagnosis

If the history suggests a hernia that cannot be demonstrated clinically by plain abdominal X-ray or US, an abdominal CT should be considered, which may detect subclinical hernias [227]. The diagnostic approach is the same as for other causes of obstruction (see Chap. 18).

#### 19.5.5 Treatment

##### 19.5.5.1 Conservative Treatment

In the absence of emergency indications, conservative treatment is preferred with rest, weight control, abdominal binders, and stool softeners [160]. Repair should be deferred until postpartum uterine involution and the restitution of the abdominal wall change due to pregnancy (see Sect. 19.6.1).

##### 19.5.5.2 Emergent Operation

Prevention and management of fluid and electrolyte imbalances are a challenge for a pregnant woman with an obstructed ileostomy who has lost the absorptive functions of the colon. Fluid and electrolyte substitution is necessary even if the patient is not vomiting due to intraluminal fluid accumulation. This is started during the diagnostic workup.

Indications for emergent operation are the same as for other abdominal wall hernias in pregnancy—incarceration, strangulation, or perforation [228]. Recognition of the obstruction requires immediate relief, generally by nasogastric suction or surgical intervention. Peristomal erythema and tenderness require emergent management. An obstruction with these skin changes is highly suspicious of bowel perforation in a hernia. Other diagnoses should be presumed without obstruction as an abscess or necrosis from different primary diseases. An emergent operation is also indicated, but different surgical procedures are performed depending on the underlying cause. Cephalosporins (FDA category B) are introduced 30 min before incision and continued if indicated by intraoperative findings. With incarcerated organ perforation (especially if contents are spilled into the free abdominal cavity) or obstruction of the large bowel, metronidazole (FDA category B) should be administered.

There are several techniques for the elective repair of different types of hernia: open suture, open mesh, or laparoscopic mesh. In nonpregnant women, a higher reoperation rate after inguinal hernia repair is not related to a particular technique. Consequently, the routine use of open mesh methods in females is not recommended [229]. The situation is similar to an emergent situation. If the incarcerated content is the bowel, vitality is most important. The gangrenous bowel should be resected, while resection is not mandatory for gangrenous fallopian tubes or ovaries (see Chaps. 6 and 7). With gangrenous or perforated bowel, hernioplasty with mesh is contraindicated because of a significant increase in wound infection rate. Suture techniques are still widely used to repair umbilical hernias, with a 20% recurrence rate [87]. Thus, mesh repairs are performed more frequently with lower recurrence rates. There are no definitive conclusions regarding technique, material, or mesh position. Surgical options for repair include peristomal hernia repair with or without mesh or stomal transposition with or without mesh repair. Open or laparoscopic access is allowed.

## 19.6 Diastasis Recti Abdominis

### 19.6.1 Abdominal Wall Muscle Changes During Pregnancy

The linea alba, the complex connective tissue, which connects the left and right abdominal muscles, is mainly affected by the expansion of the abdomen [230]. The width of the linea alba is the inter-recti distance and varies along its length from the xiphoid to the pubic symphysis. In women between 20 and 45 years of age, the width of the normal linea alba is highly variable. The mean US width was  $7 \text{ mm} \pm 5 \text{ mm}$  (at xiphoid),  $13 \text{ mm} \pm 7 \text{ mm}$  (3 cm above the umbilicus), and  $8 \text{ mm} \pm 6 \text{ mm}$  (2 cm below the umbilicus) [231]. Diastasis recti abdominis (DRA) is diagnosed when the width exceeds these values. The inter-recti distance decreases markedly from day 1 to 8 weeks. Without any intervention (e.g., exercise training or physiotherapy), there is no further closure at the end of the first year [231].

The gross structure of the rectus abdominis muscle is altered during pregnancy. Significant increases happen in muscle length, separation, and angles of insertions as the pregnancy progresses [232]. The functional ability of the abdominal muscles is also altered, and the ability to stabilize the pelvis is decreased. Upper rectus abdominis relatively integrated electromyography (EMG) increased while external oblique and lower rectus abdominis relatively integrated EMG decreased for all abdominal exercises. Relative EMG for all tested muscles returned to levels seen at 18 weeks and 26 gestations by 18 weeks post-birth. Functional changes are found in the rectus abdominis and external and internal obliques. During the immediate post-birth period, separation of the rectus abdominis was resolved by 4 weeks post-birth, and abdominal muscle inter-relationships returned to early pregnancy levels by 8 weeks postpartum. However, the ability to stabilize the pelvis remained low at 8 weeks postpartum. This sustained decrement in the ability to stabilize the pelvis at 8 weeks postpartum may reflect the poor resolution of abdominal muscle length increases due to pregnancy [232].

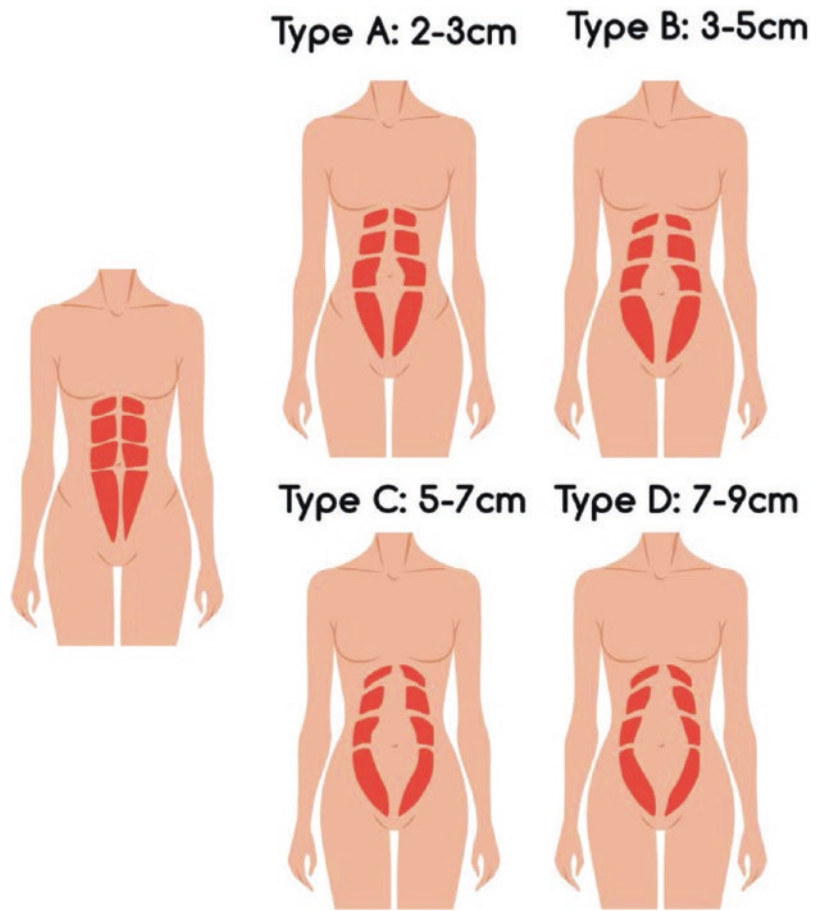
Another issue that may affect hernia repair is hormonal changes during gestation. Relaxin is a peptide hormone in the insulin family secreted by the corpus luteum [233]. It is also released from the placenta during pregnancy. It relaxes pelvic ligaments. Relaxin reduces extracellular matrix (ECM) synthesis, causes degradation by metalloproteinases [234], and induces collagen degradation [235], causing a significant reduction in tissue collagen content [236].

### 19.6.2 Incidence and Risk Factors

There is little research about DRA and its relation to pregnancy. Around 27% of women have a DRA in the second trimester and 66% in the third trimester of pregnancy. Around 53% of these continued to have a DRA immediately postpartum, and 36% remained abnormally wide at 5–7 weeks postpartum [91]. DRA existed in 33.1, 60.0, 45.4, and 32.6% of the women at 21 weeks of pregnancy and at 6 weeks, 6 months, and 12 months following delivery, respectively [237].

DRA is observed in the second trimester. Its incidence peaks in the third trimester. It remains high in the immediate postpartum and declines but does not disappear in the later postpartum [238]. None of the subjects had a DRA below the umbilicus without at or above the umbilicus. Only subjects with a DRA below the umbilicus were in the third trimester of pregnancy [238]. The anterior aspect of the rectus sheath is presumed to be stronger below the umbilicus because the aponeuroses of all four muscles of the anterior abdominal wall cross in front of the rectus abdominis muscle below the arcuate line. The DRA is defined as the separation greater than two finger widths. Above the arcuate line, the two sides of the rectus abdominis muscle are about 2 cm apart but only about 1 cm apart below that line. The two bellies of the rectus abdominis musculature resemble a “v” as they approach their insertion at the pubis. Therefore, the criterion of greater than two finger widths may not be appropriate below the arcuate line (i.e., below the umbilicus). Diastasis recti classification is presented in Fig. 19.47.

**Fig. 19.47** *M. rectus abdominis* position changes before, during, and after pregnancy. (Reproduced with permission from [239] under the CC BY 4.0)



General risk factors for abdominal wall hernia are presented in Table 5.1. The risk for DRA is twofold higher in women reporting heavy lifting 20 times a week or more. The weight of a baby is about 8 kg at 6 months and 10 kg at 12 months. These weights raise intra-abdominal pressure as high as a Valsalva maneuver. In the urogynecological population, 52% of patients have DRA [125]; 66% of these women had at least one support-related pelvic floor dysfunction (stress urinary incontinence, fecal incontinence, or pelvic organ prolapse). There is a positive correlation between parity and DRA [240]. Decreased incidence in the early postpartum period, compared to the third trimester [238], refutes an idea (R. Kotarinos, personal communication, 1985) that the increased intra-abdominal pressure exerted during the second stage of labor (i.e., when the baby is expelled from the mother's

uterus) is a primary cause of separation. DRA is absent in women who had been conscientious exercisers before pregnancy [238].

### 19.6.3 Classification

Clinically, it appears that there are two subgroups of postpartum women with DRA:

- Those who, through a multi-modal treatment program, can restore optimal strategies for transferring loads through the abdominal canister with or without achieving closure of DRA,
- Those who (a) despite apparently being able to restore optimal function of the deep muscles (optimal neural system) and who (b) do not have a loss of articular integrity of the

joints of the low back or pelvis (optimal articular system) and in whom (c) the inter-recti distance remains greater than normal (non-optimal myofascial system), fail to achieve optimal strategies for transferring loads through the abdominal canister. In multiple vertical loading tasks (single-leg standing, squatting, walking, moving from sitting to standing, and climbing stairs), failed load transfer through the pelvic girdle or hip joint is consistently found.

### 19.6.4 Clinical Presentation

Most patients either do not have symptoms except a bulge on the anterior abdominal wall or symptoms disappear during the first year postpartum. It is rarely apparent during pregnancy but is visible after delivery. The confirmatory test is when a laying woman elevates the upper part of the body (Fig. 19.48). Ellipsoid bulging in the midline is visible. 52% of DRA is located at the umbilicus, 36% above the umbilicus, and 11% below [238].

### 19.6.5 Diagnosis

The diagnosis is clinical. There is no need for further workup.



**Fig. 19.48** Final position for the testing of a diastasis recti abdominis. A bulge is visible cranial to the examiner's hand. (Reproduced with permission from [238])

## 19.6.6 Treatment

### 19.6.6.1 Conservative Treatment

DRA is an impairment but not a true hernia without risk of incarceration. Asymptomatic patients should exercise to strengthen the anterior abdominal wall.

### 19.6.6.2 Surgical Treatment

#### Indications

- The woman should be at least 1 year postpartum [231]. A proper multi-modal program for restoring effective load transfer through the lumbopelvis [241] has failed to restore optimal strategies for function and resolve lumbopelvic pain or UI,
- The inter-recti distance is greater than the mean values, and the abdominal contents are palpated through the midline fascia,
- Multiple vertical loading tasks reveal failed load transfer through the lumbopelvic failure to control segmental or intrapelvic motion (SIJ/pubis symphysis) during single-leg loading (stork or one-leg standing test) [242, 243] and failure to control segmental or intrapelvic motion (SIJ/pubis symphysis) during a squat or sit to stand task [241],
- The active straight leg raise test is positive [244]. The effort to lift the leg improves with an approximation of the pelvis anteriorly and approximating the lateral fascial edges of rectus abdominis,
- The articular system tests for the passive integrity of the joint of the low back or pelvis (mobility and stability) are normal,
- The neural system tests are normal. The individual can perform a co-contraction of transversus abdominis, multifidus, and the pelvic floor. However, this co-contraction does not control the neutral zone motion of the joints of the lumbopelvis, which demonstrated failed load transfer loading [241].

The second subgroup of postpartum women has often sustained significant damage to the midline fascial structures, and sufficient tension can no longer be generated through the abdomi-

nal wall for the resolution of function. A surgical abdominoplasty to repair the midline abdominal fascia (the linea alba) is warranted for this subgroup.

## Techniques

After delivery, all techniques used in the general population apply to postpartum women. The combined repair is recommended because many women have a concomitant umbilical hernia (Table 19.3). Although two-row suture plication with delayed absorbable material provides similarly good results with retromuscular lightweight polypropylene mesh without an increase in recurrence rate in the treatment of DRA [245], mesh use results in lower recurrence in patients with a concomitant umbilical hernia and DRA [246]. A recurrence may develop from the sites of mesh fixation if there is a vulnerable linea alba due to DRA. Therefore, it is better to use no fixation in case of strong restoration of the line alba or to use an atraumatic mesh fixation like glues (e.g., fibrin) [247] or a self-gripping mesh in retromuscular mesh repairs [248]. The best results, including cosmesis, result from the laparoscopic extraperitoneal Rives-Stoppa procedure using nonabsorbable mesh.

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# Symptomatic Diaphragmatic Hernia

# 20

## Abstract

A diaphragmatic hernia is a rare condition during pregnancy, but the symptomatic form carries high maternal and especially fetal mortality. Nonspecific symptoms are commonly attributed to other diseases, especially because clinicians are reluctant to use plain chest X-ray, which is often diagnostic. The use of thoracic sonography and thoracic MRI add to an earlier and more accurate diagnosis. In most cases, present immediately after labor and abdominal or thoracic CT can be performed with high diagnostic accuracy. For a symptomatic patient, treatment is surgical, mostly at the time of presentation. A treatment algorithm is less straightforward for asymptomatic patients detected during pregnancy. Some recommend surgical treatment to prevent complications during labor when increased intra-abdominal pressure occurs, while others operate when symptoms develop. The type of delivery is also not solved completely. Some recommend Cesarean section at 34 weeks with simultaneous diaphragmatic hernia repair. Others claim that vaginal delivery is safe with laparoscopic diaphragmatic hernia repair postpartum.

## 20.1 Historical Perspective

Sennertus, in 1541, described the first case of a diaphragmatic hernia (DH). Ambrose Paré, in 1575, described the first two deaths, one from a strangulated bowel [1, 2]. In 1834, French physician Rene Laennec suggested that the diagnosis of DH could be made by chest auscultation and that a laparotomy could be used to withdraw the intestine from the thorax. Naumann, in 1888, made the first unsuccessful reduction of a DH in the general population by laparotomy [3]. In 1889, O'Dwyer [4] reported another unsuccessful strangulated congenital DH (CDH) repair. Riolfi performed the first successful repair in 1886. In 1905, Heidenhain [5] reported a successful congenital CDH (CDH) repair in 1902 in a 9-year-old patient. He reduced a hernia and closed the diaphragmatic defect through a mid-line laparotomy incision.

Walter Gray Crump (Fig. 20.1) made the first available report on the successful operative treatment of DH at 3 months gestation in 1911 [7]. Müller, in 1913, made one of the first descriptions of incarcerated DH during puerperium [8]. Ude and Rigler, in 1929, observed the risk factors such as multiple pregnancies, large ovarian cysts, large myomas, and ascites with malignancy [9].



**Fig. 20.1** Walter Gray Crump (1869–1945), an 1895 graduate of New York Homeopathic Medical College. Later, he continued to work for the college as a professor of surgery and achieved emeritus status. He established the first scholarship for African American medical students at the same college in 1928. He was also a trustee at Howard University and Tuskegee Institute, the first college founded to educate African American clergymen and then expanded into a university of liberal arts and medicine [6]

Campos and Sipes, in 1991, made the first laparoscopic repair in the general population [10], while Watkin et al. made the first laparoscopic repair in puerperium in 1993 [11].

## 20.2 Incidence and Etiology

### 20.2.1 Acute Diaphragmatic Fatigue

Acute diaphragmatic fatigue occurs in healthy subjects and patients with chronic obstructive pulmonary disease by modifying their breathing pattern or breathing against high inspiratory resistances. During the expulsive period of labor, women are asked periodically to make strong expulsive efforts and sustain them isometrically

for many seconds; this is likely to produce “natural” diaphragmatic fatigue. The development of diaphragmatic fatigue is assessed by measuring the static maximal inspiratory pressure and analyzing the electromyographic power spectrum of the diaphragm.

These findings demonstrate that (1) the diaphragm is active in the expulsive efforts during labor, and (2) the tension developed and the time each contraction is maintained may lead to the development of diaphragmatic fatigue. Therefore, evidence suggests that acute diaphragmatic fatigue is a natural condition [12].

### 20.2.2 Diaphragmatic Eventration

Diaphragmatic eventration (Jean Louis Petit, 1790) is an elevation of a hemidiaphragm without defects in continuity. The muscular insertions are normal, the normal orifices are sealed, and there is no interruption of the pleural or peritoneal layers [13]. It is due to a thin floppy attenuation of a portion of the diaphragm that allows the intra-abdominal viscera to push the diaphragm upward to encroach the lungs.

In most cases, the diaphragm eventration is on the left side. During surgery, the most common cause is phrenic nerve injury secondary to trauma, infiltration, or neoplastic or iatrogenic compression. Those of congenital origin is caused by a partial or total lack of muscles in the pleuroperitoneal membrane, associated with chromosomal abnormalities and prematurity [14]. Eventration of the diaphragm produces its weakening and a higher risk of rupture with an increase in intra-abdominal pressure, as it occurs during pregnancy—repeated vomiting, a rapid increase in the uterine size, and the Valsalva maneuver during labor [15, 16].

### 20.2.3 Diaphragmatic Hernia

DH is a defect in the diaphragm (the muscle that separates the chest cavity from the abdominal cavity). Astley Cooper has classified DH into [12]:

- *Congenital*, defects in the diaphragm arising from the faulty embryologic development,
- *Acquired*, develops at points of anatomic weakness, e.g., at the esophageal hiatus, aortic, or caval openings,
- *Traumatic*, rents in the diaphragm arising from direct or indirect trauma.

From 1928 to 1953, 54 patients with DH in pregnancy were reported in English literature [17–22], and up to 2011, around 80 cases [18, 23]. One review reports the following declining incidence: the third trimester at 50%, the second trimester at 37%, and the puerperium at 13% [24]. It is more commonly discovered in multiparas [24]. CDH is present in 30%, positive traumatic history in 40%, and the unknown cause in 30% [24]. Abdominal organs involved in DH, in decreasing order, are the colon (77%), stomach (57%), small intestine (30%), greater omentum (23%), spleen (13%), and liver (7%) [24]. In another review, 54% presented after 24 weeks gestation, 21% before 24 weeks, 20% during labor or postpartum, and 5% did not report gestation [25].

### 20.2.3.1 Congenital

CDH occurs when the diaphragm does not form completely, leaving a hole. If the defect is in the posterolateral aspect, then it is called the hernia of Bochdalek. If it is in the presternal (parasternal) region, then it is called the hernia of Morgagni–Larrey [26]. Morgagni DH results from a small defect between the attachment of the diaphragm to the xiphoid process and the 7th costal cartilage—the muscle-free space called the Larrey space.

The incidence of asymptomatic Bochdalek's hernia in the adult population is at least 0.17%, with a female-to-male ratio of 3:1 [22]. Parasternal or Morgagni–Larrey hernias are rare, comprising 2.5–3% of all CDH. Despite such a high incidence in the general population,

the number of pregnancies complicated by unrecognized CDH is extremely small. Despite claiming the prevalence in the general population of 1/2000–1/5000 live births [27], less than 100 cases during pregnancy have been reported since 1928 [24, 25, 28]. The pathogenesis of CDH is unclear in many cases, caused by gene mutations indicating that CDH is etiologically heterogeneous [27]. Other causes are toxins (pesticides, nitrofen) which cause increased expression of vascular cell adhesion molecule [29], decreased expression of vascular endothelial growth factor [30], and downregulation of fibroblast growth factors 7 and 10 [31]. Hernia of Bochdalek is the most common type of CDH. The posterolateral defect occurs in the left hemidiaphragm in 90% [24, 28] of cases because (1) the right diaphragmatic space is stronger, (2) it is protected from a sudden increase in abdominal pressure by the liver, and (3) the right canal closes before the left [32, 33]. CDH hernia repaired before pregnancy could be a risk factor for the recurrence of CDH during pregnancy [34].

Of the 56 cases identified, 54% presented after 24 weeks gestation, 21% before 24 weeks, 20% during labor or postpartum, and 5% did not report gestation [25].

### 20.2.3.2 Traumatic

#### Penetrating Trauma

Traumatic diaphragmatic injuries frequently occur after penetrating thoracoabdominal trauma. The reported incidence is up to 19% [27, 35]. Penetrating knife wounds in the chest usually result in pneumothorax or hemothorax. Most will resolve with the insertion of a chest drain without a thoracotomy. Injuries on the left side of the chest wall below nipple level (5th intercostal space) are at risk of injuring the diaphragm. Many will be asymptomatic and present from 2 weeks to 40 years after the original injury [33, 36]. Ideally, a follow-up chest X-ray should be performed weeks after recovery from the index injury since abnormalities are present in 94% of cases [37].

### Blunt Trauma

Diaphragmatic rupture after blunt trauma is less common, with an incidence of 5% [38]. About 88% of blunt diaphragmatic injuries result from motor vehicle accidents [39]. Blunt trauma increases intra-abdominal pressure. The compression of the abdominal contents causes a bursting force under the surface of the diaphragm, resulting in a linear tear in the line of the fibers from the region of the left central tendon toward the esophageal ring, but rarely into intact abdominal viscera for its transmission [40]. The thoracic cage is rarely extensively damaged. If any ribs are fractured, they are usually below the level of the 8th. This fact is also consistent with the force acting from the abdomen rather than the chest.

In nonpregnant patients, 90% of these hernias occur on the left side because the liver protects the right side, and the left hemidiaphragm is weaker [33]. In the general population, lateral impact motor vehicle collision victims are more likely to experience a diaphragmatic rupture than victims of frontal collisions. Occupants exposed to left lateral impacts are at the greatest risk. The side of diaphragmatic rupture correlates with the direction of impact. Deformation shear is a more plausible mechanism for diaphragmatic rupture after lateral impacts [41]. Spontaneous healing after the injury is unlikely because the diaphragm is in constant motion. Usually, there is no pneumothorax, hemopneumothorax, or subcutaneous emphysema, and there are common presentations in severe injuries to the upper chest. The DH becomes evident mostly in advanced pregnancy [42].

Strangulation of abdominal viscera in a preexisting congenital or traumatic diaphragmatic defect is more common than in spontaneous rupture of the diaphragm [43–45].

### Iatrogenic

The third cause of traumatic DH is iatrogenic. Usually, it results from thoracoabdominal surgery, such as esophagogastric surgery for esophagus cancer, gastric cancer, achalasia [46], or extensive oncologic operations in the upper abdomen [47]. There are several mechanisms.

The paraesophageal DH most likely resulted from a weakness in the diaphragm from the myotomy surgery [48, 49]. Widening of the esophageal hiatus in the diaphragm could have resulted/worsened from the short interval from myotomy to pregnancy, increased abdominal pressure from the enlarging uterus, hyperemesis, and increased progesterone levels. How pregnancy might affect the healing of a myotomy scar or how long to wait before it is safe to get pregnant is unknown. Another mechanism is that an unnoticed tear occurred during the previous splenectomy or that the left leaflet was weakened by the hemorrhagic surgical procedure [44]. Since this patient's surgery, repeated increases in intra-abdominal pressure (caused by coughing, sitting positions, constipation, and straining) likely enlarged the unnoticed tear or contributed to further stretching of the weakened diaphragm fibers resulting in a rent. Pregnancy provides additive factors of increased intra-abdominal pressure: nausea and vomiting until the 16th week and the enlarged pregnant uterus in the second trimester. With advancing pregnancy, as the uterus enlarges, it forces an increasing amount of abdominal content into the chest. All these factors may convert an occult defect to symptomatic and increase the risk of twisting and torsion of herniated viscera.

### Spontaneous Rupture During Labor

Spontaneous rupture of the diaphragm during normal vaginal labor is extremely rare. It could result from a sudden sharp rise in the intra-abdominal pressure during the second stage of labor, exacerbated by external pressure to the uterine fundus or the upper abdomen. The pathophysiological mechanism is similar to spontaneous rupture during a cough; sometimes, it is difficult to detect which causes spontaneous rupture of the diaphragm. A cough has three different phases: (1) the inspiratory phase, (2) the compressive phase, and (3) the expulsive phase [50].

A sudden sharp rise in the intra-abdominal pressure during vaginal labor is similar to the first and second phases of the coughing process. The inspiratory phase starts with a deep inspiration resulting in increased lung volumes and elastic



recoil pressure. During the compressive phase, the glottis is closed, and the expiratory muscles contract. Resultant intrathoracic pressure increases to generate high-velocity flows for the expulsive phase of a cough. The glottis opens with the expulsive phase, and the high-pressure gradient generates rapid airflow. Both inspiratory and expiratory muscles are active in coughing. Extreme intrapleural pressure changes occur from the active contraction of these muscles [51]. Two different theories can explain the fracture of ribs from excessive strain during a cough. The first mechanism of rib fracture in cough is similar to that of stress fractures [52]. With force (muscle contraction), an object (a rib) is subjected to stress. The stress causes the deformation of the object. When the deformation exceeds the elastic limit of the object, it undergoes inelastic deformation. Repeated trauma, as in cough outbreaks, can produce inelastic deformation in the most vulnerable part of the ribs, the middle third. This will initially result in minor cracks of the ribs and later in fractures as the trauma continues. Fractures can occur in any rib. The most commonly involved are the fifth to tenth ribs [52]. The second mechanism of rib fracture may be due to opposing muscle forces acting on the ribs.

The diaphragm is mainly an inspiratory muscle. The costal part of the diaphragm is attached to the lower six ribs and their cartilage. The muscles of expiration are the chest wall muscles, including the internal intercostals, the triangularis sterni, the serratus posterior, the quadratus lumborum, and the abdominal muscles (including the external and internal oblique, the rectus abdominis, and the diaphragm) [53]. The diaphragm also acts as an expiratory muscle during activities requiring high intrathoracic pressure, like coughing, vomiting, and sneezing [51]. This expiratory activity of the diaphragm is related directly to intrapleural pressure and follows the expiratory activity of the transversus abdominis muscle. It is speculated that the diaphragmatic contraction stabilizes the thoracic cavity during a cough's expulsive phase. A fracture line starts 4 cm from the costochondral junction of the fourth rib, running obliquely caudal and laterally

to the ninth rib in the midaxillary line [53]. This line falls on the muscular attachments of the external oblique and serratus anterior muscles. The opposing actions of these muscles on the same ribs can result in fractures. Simultaneous contraction of the shoulder girdle muscles, especially of the serratus anterior, also contributes to rib fractures by pulling the ribs upward and laterally. In contrast, the abdominal muscles pull the ribs medially and downward [53].

The development of a hernia during pregnancy is multifactorial, relating to the mass effect of the gravid uterus, smooth muscle relaxation, and softening of ligaments. Obstructive shock during labor increases venous blood return to the heart due to the spontaneous contractions of the uteroplacental circulation, the release of the catecholamine in response to labor pain, the autotransfusion from the contracted uterus, and the release of the aortocaval compression occurring during labor or immediate postpartum period [54, 55]. All reported cases of "spontaneous" rupture in pregnancy are left-sided. There are seven spontaneous ruptures during labor [16, 44, 45, 56–59], all on the left side. Causes of the abrupt and excessive increase of intra-abdominal pressure, such as coughing in patients at risk, especially chronic obstructive pulmonary disease or vomiting, could also cause a spontaneous rupture that could become evident during pregnancy or labor or even early postpartum [57]. Spontaneous rupture of the diaphragm associated with vaginal delivery happens regardless of age, obstetric history (primigravida or multigravida), or DH history. Diaphragmatic defects range from 3 cm to a large unmeasured tear (the hiatus to the chest wall). Larger tears tend to be associated with mediastinal shifts [56].

### 20.2.3.3 Hiatal Hernia

Hiatal hernias (HHs) are herniations of parts of the abdominal contents through the esophageal hiatus of the diaphragm. HH is six times more common in pregnant patients than the other two types [26, 47] and occurs in up to 18% of multipara and 5% of primipara [22]. There are four types as follows:

**Type I (sliding)**, the most common type, is characterized by widening the diaphragm's muscular hiatal aperture with laxity of the phreno-esophageal membrane, allowing some of the gastric cardia to herniate upward. A sliding HH is probably related to the loss of elasticity of these ligaments caused by excessive contraction of the longitudinal esophageal muscles, increased abdominal pressure, genetic predisposition, and age-related degeneration.

**Type II (paraesophageal)** results from a localized defect in the phreno-esophageal membrane. The gastroesophageal junction remains fixed to the preaortic fascia and the arcuate ligament, and the gastric fundus forms the leading part of the herniation. Paraesophageal HH represents 5% of all HHs [22]. This condition is rare before the fourth decade of life; however, the patients involved are generally 20 years older than those with a sliding HH, suggesting that this is an acquired disease, evolving over the years [60]. These are true hernias surrounded by a peritoneal sac, and when the defect is large, incarceration with obstruction, gastric volvulus, or strangulation may occur [26, 61, 62].

**Type III** hernias are a mix of types I and II.

**Type IV** is also called *complex HH*.

Incidence varies considerably due to different inclusion criteria. In asymptomatic patients, the incidence depends on the duration of pregnancy. Until the 16th week of gestation, the incidence is 0.9%, and when women with negative findings were restudied in the 34th week of gestation, the incidence of HH was 7.2% [63]. From 1903 to 1951, 19 cases of HH complicating pregnancy were published [64], while from 1928 to 2012, 38 cases were in the English literature [65–67]. The median age was 28 years, and 67% were multiparous [65]. In 1934, small hernias through the esophageal hiatus in the third trimester of pregnancy were found in 18.1% of multiparas and 5.1% of primiparas (12.1% combined). In 30% of the small DH, the defect was not demonstrable after parturition [22].

## 20.3 Clinical Presentation

The clinical presentation of maternal DH during pregnancy varies. The three most common manifestations of DH are [25] as follows:

- Abdominal or chest pain (84%),
- Vomiting (60%),
- Dyspnea (41%).

Auscultation of bowel sounds on chest examination is highly indicative of a DH. Nevertheless, a physical examination is usually not enough for diagnosis.

Some claim that patients with DH symptoms during pregnancy did not have symptoms before pregnancy [24], probably because their diaphragm defects were too small to cause symptoms.

### 20.3.1 Diaphragmatic Eventration

As more than 50% of adult patients remain asymptomatic, this condition often goes undiagnosed. The other 25% of patients have only mild exertional dyspnea. In DH, *Litten's sign* may be absent, and the line of tympany may be less movable than in diaphragmatic elevation. Pregnant women with eventration of the diaphragm can become symptomatic during labor [68]. After labor, lung and diaphragm functions return to normal [68].

Clinical examination of diaphragmatic eventration reveals dullness on percussion and absent or decreased breath sounds over the lower chest on the involved side. On deep palpation, the inspiratory excursion of the abdomen is less on the paralyzed side, but paradoxically, the lower rib cage shows greater excursion on the side of paralysis. The diaphragmatic muscle is thin and weak with reduced, paradoxical, or absent movement on fluoroscopy and sonography (US).

### 20.3.2 Hiatal Hernia

Rigler and Eneboe, in 1935, showed that the association of HH with pregnancy is common. However, they could not demonstrate any correlation between gastric symptoms and the presence or absence of a hernia [22]. Women may be asymptomatic until pregnancy, when further herniation is caused by increased stress on the diaphragm by repeated vomiting in the first half of the pregnancy, a rapidly enlarging uterus in the second trimester, and Valsalva maneuvers during labor. The symptomatic phase includes flatulent dyspepsia, postprandial substernal discomfort relieved with vomiting, reflex cardiac irregularities (tachycardia and arrhythmia), and dysphagia. Some form of nausea and vomiting occurs in up to 80% of pregnant women in the first trimester. Recurrent vomiting in the second or third trimester is associated with epigastric pain and retching of blood-stained fluid, which may proceed to frank hematemesis and melena. Also, respiratory symptoms should raise the suspicion of complicated DH. If the disorder is complicated by reflux esophagitis, which is common, then there may be intense “burning pain” behind the lower end of the sternum, which may radiate up to the neck. There may be slight dysphagia, and a gastric ulcer may develop near the cardia. Retching of blood-stained fluid may proceed to frank hematemesis and melena. Strictures may develop at the lower end of the esophagus. Porter Vinson was the first to note the association between vomiting in pregnancy, esophagitis, and stricture. Probably an HH was present during pregnancy [69]. With the progression of DH, potentially fatal complications could occur, such as obstruction, torsion, strangulation, or infarction of the herniated viscera [47]. In 1940, it was stated that the resolution of symptoms is rapid in the puerperium and attempts to make a postpartum diagnosis may be unsuccessful because of the diminution in the size of a hernia or even its disappearance [70].

With elective presentation, HH should be suspected if:

- Symptoms persist after 12 weeks of pregnancy,
- The symptoms occur after the first trimester.

### 20.3.3 Posttraumatic Hernia

The emergent clinical presentation after trauma consists of a combination of the mechanical effect on the cardiorespiratory function by the displaced viscera and the pathological changes in the viscera themselves consequent upon their displacement. The clinical entity is readily divided into three phases (no first phase in CDH) [71] as follows:

1. Immediately following trauma,
2. Quiescent period,
3. Associated with strangulation.

1. The early symptoms and signs become confused owing to the diversity of injuries likely to be associated with this condition: pain in the left chest or left upper back [72], pain in the left upper quadrant of the abdomen, left shoulder tip pain, vomiting, and shortness of breath associated with shock [71]. Even minor trauma in a patient with a predisposition, such as a heavy cough or difficult defecation, can cause DH [72]. An expanding mass in the chest may displace mediastinal structures with compression of the vena cava, impairing venous return and producing hypotension [54]. Compression and displacement of the lung cause the striking collapse of the lungs (atelectasis), which leads to hypoxia and dyspnea [57]. There is usually diminished air entry to a varying degree at the affected base, and the percussion note may be impaired or unduly tympanic. Tenderness and rigidity are common in the left upper quadrant of the abdomen. All left-sided lesions have demonstrated the consistency of this picture. Therefore, if the X-ray suggests elevation of the left leaf of the diaphragm above its normal position, particularly if there are a large gas bubble and fluid level in the erect position, in a patient involved in the accident, then the findings are pathognomonic of the ruptured diaphragm. The sequence of events from this point varies considerably. The lesion may continue directly to strangulation with a false

“quiescent” period of only a few hours or may pass into a true quiescent phase, which may last up to several years. If strangulation follows immediately on the trauma, then this is characterized by intractable vomiting. The vomitus may be of a non-bile-stained material or in the form of repeated hematemesis or merely dry retching. Severe pain develops in the left chest, left upper quadrant of the abdomen, and left shoulder tip. The patient becomes profoundly shocked and rapidly moribund. The diaphragm’s elevation and the gas bubble’s size are likely to be greater with strangulation than in nonobstructed cases. When none was present, the aspiration of serosanguinous fluid from the chest strongly suggests strangulation. It is vital to recognize the onset of strangulation because if gangrene occurs, then the mortality, even with the operation, approaches 100% compared to almost none in the absence of obstruction [73].

2. It is more common for the lesion to pass into a “quiescent” phase in response to the treatment of shock. The improvement may be so rapid that the medical attendant is completely hoodwinked only into being rudely awakened by the sudden onset of strangulation after hours, days, months, or years. If the quiescent phase is prolonged, then there may be no symptoms or only vague symptoms, such as shortness of breath on exercise or in advanced pregnancy due to increased intra-abdominal pressure [74], substernal discomfort after meals, vague upper abdominal discomfort, sometimes relieved by vomiting or attacks, or subacute intestinal obstruction. These symptoms may be insufficient to make the patient seek medical attention,
3. Strangulation is one of the most severe complications of DH. The onset of strangulation occurs most commonly within 3 years of the injury, and its onset is usually sudden. It may follow raised intra-abdominal pressure due to unwanted straining or spontaneously in the later months of pregnancy. In many cases, a traumatic hernia is unsuspected, and the history of a previous accident may not be volunteered. The presence of intestinal obstruction

is probably recognized. However, in the absence of abdominal distension and with the bizarre upper abdominal, chest, and shoulder tip pain pattern, conservative management may be continued for too long. There are cases where the compression of the left gastric vessels by the intact esophageal ring appeared to play a major part in the causation of gangrene. More commonly, gangrene is associated with “direct” DH when the opening is smaller. Rare cases have been reported with a normal X-ray immediately after admission, but herniation and even strangulation occurred later. It is presumed in these circumstances that the greater omentum or the spleen temporarily covered the opening but raised intra-abdominal pressure later caused the herniation.

The presentation on the right side may be quite different from that on the left in that bowel is rarely herniated into the chest unless the tear is large, and consequently, the risk of strangulation is minimal. The symptoms of cardiorespiratory dysfunction are due to the gross displacement of the lung, the paradoxical movement of the viscera through the large opening, and the gross loss of function of the right half of the diaphragm. Even cardiac arrest could result from direct compression and mediastinal shift [75, 76].

The main complications include visceral obstruction [26, 44], spontaneous [45, 57] or thoracocentesis-induced [43, 77] visceral perforation, visceral strangulation with or without subsequent gangrene, and perforation/rupture [15], maternal respiratory distress [11, 57, 78], tension pneumothorax [77], tension gastrothorax [79], and maternal death [80]. They are more frequent during the third trimester, delivery, and early puerperium.

The intrathoracic organ perforation includes nonsolid organs such as the stomach and small or large intestine. Clinical presentation depends on the underlying pathophysiology. If strangulation precedes perforation, then intense acute abdominal and thoracic pain is followed by fever and shock. Without strangulation, gastric perforation from a peptic ulcer can be caused due to exces-

sive use of painkillers. Such presentation can be subacute (3–5 days) and characterized by severe epigastric pain, moderate but worsening dyspnea, and fever [81].

Frank Scott Gibson, in 1929, stressed the following diagnostic symptoms of strangulated DH in the general population [82], which apply to the pregnant population as follows:

- Diminished expansion of the chest,
- Impairment of resonance,
- Adventitious sounds,
- Cardiac displacement,
- Circulatory collapse,
- Cyanosis and dyspnea,
- Asymmetry of hypochondria.

Sometimes patients can hear a gurgling sound from the stomach or intestine in the chest. Diminished breath sounds on the ipsilateral side are the most common physical finding [83, 84]. The absence of abdominal distension is present when the stomach, unaccompanied by the intestine, is herniated through the rent in the diaphragm. Sometimes, peristalsis results in audible bowel sounds during chest auscultation.

It is important to suspect traumatic DHs in patients with dyspnea or bowel obstruction with a previous chest or abdominal trauma. Small scars can be hidden below breasts, in the inframammary fold, etc. In such cases, the clinician does not suspect previous diaphragmatic injury [85].

### 20.3.4 Congenital Diaphragmatic Hernia

CDH occurs most commonly during periods of elevated intra-abdominal pressure. In pregnancy, this period is present during the third trimester, vaginal delivery (especially with prolongation of the second stage of labor), or early postpartum [20]. Clinical presentation is similar to the second or the third phase of posttraumatic DH or a combination of these two clinical phases. During vaginal delivery or early puerperium, a common combination of abdominal and respiratory symptoms exists. The presentation is persistent nausea,

vomiting (gastric, bilious, or feculent), epigastric pain, inability to pass flatus or stool if the intestinal obstruction is complete, or new-onset dyspnea with pleuritic-type chest pain with radiation to the shoulder tip or back, tachypnea, cyanosis, and pallor. Early in the course of the disease, before hollow viscus perforation, the patients are afebrile. This should raise the suspicion of DH. The interval between the onset of symptoms and surgery ranges from 10 to 48 h [56, 86]. Sometimes, these symptoms and signs are present before or during pregnancy, but in less exaggerated form, patients take them as normal side effects of pregnancy [84].

## 20.4 Differential Diagnosis

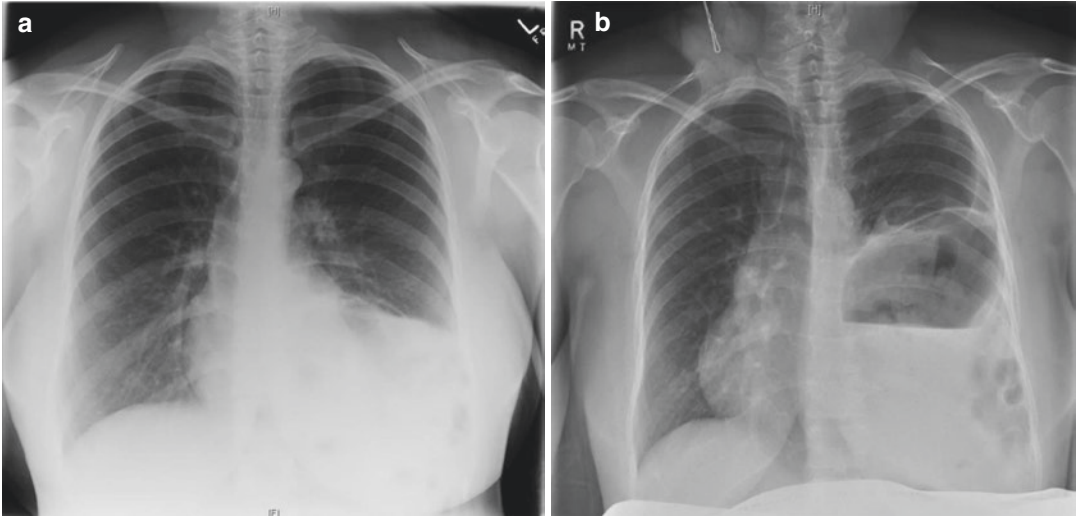
Mild symptoms of maternal DH can imitate hyperemesis gravidarum or achalasia [46]. Pregnancy can make diagnosing achalasia more difficult as the increased progesterone levels relax the lower esophageal sphincter, decreasing its resting tone and alleviating some symptoms [87].

The absence of fever or a cough helps differentiate DH from pneumonia or pleurisy. Some DHs are misdiagnosed from misreading plain radiographs (Fig. 20.2), where peritoneal fluid and bowel loops can masquerade as pyopneumothorax or pneumonia [25, 88]. When a chest X-ray suggests lower lobe pneumonia but is doubtful [25, 28], normal bronchoscopy findings suggest DH [25]. A large air-filled translucency will appear on the radiograph if the stomach or colon is herniated and filled with gas (Figs. 20.3 and 20.4). The translucency may simulate a pneumothorax or a congenital cystic lesion of the lung. If the stomach is filled with fluid, the imaging may show a large opacification containing a large translucency.

A pulmonary embolism is another similar clinical presentation, mostly without abdominal symptoms. Mostly, it is suspected after the Cesarean section (CS) [74].

Spontaneous esophageal rupture during pregnancy is rare and, when it does happen, tends to be associated with hyperemesis gravidarum in





**Fig. 20.2** (a) Chest X-ray from the first presentation at 13 weeks shows left lower lobe opacification misdiagnosed as left lower lobe pneumonia. (b) Chest X-ray from the presentation at 31 + 3 weeks shows a raised or rup-

tured left hemidiaphragm with bowel visible in the chest and displacement of the mediastinum to the right. (Reproduced with permission from [25] under the CC BY 4.0)



**Fig. 20.3** Posteroanterior chest X-ray shows a large left pleural effusion and gastric air–fluid level in the left hemithorax. (Reproduced with permission from [15])

the first trimester [89–91]. Opioid analgesia could potentiate the possibility of rupture. It impairs lower esophageal sphincter relaxation minutes after intravenous administration [91]. If not clinically evident, an infected pleural fluid with a high amylase content is consistent with that diagnosis. However, the appearance of the material aspirated has a feculent odor, and Gram stain reveals polymicrobial flora (especially *E. coli*, *Enterococcus* spp., and anaerobes), intesti-



**Fig. 20.4** Posteroanterior chest X-ray shows colonic air–fluid levels in the left hemithorax. (Reproduced with permission from [56])

nal rupture is likely [77]. If abdominal distension with (feculent) vomiting dominates, then intestinal obstruction from any cause could be causative (Table 20.1).

**Table 20.1** Differential diagnosis of a diaphragmatic hernia during pregnancy

|                           |
|---------------------------|
| Hyperemesis gravidarum    |
| Achalasia                 |
| Diaphragmatic eventration |
| Pulmonary embolism        |
| Intestinal obstruction    |
| Acute coronary syndrome   |
| Pneumothorax              |
| Pneumonia/empyema         |
| Asthma                    |
| Pleurisy                  |
| Esophageal rupture        |

## 20.5 Diagnosis

Of 30 cases, 50% were misdiagnosed because of atypical symptoms and the lack of chest radiographs [24]. Intrathoracic location of abdominal organs may mimic pleural effusion or pneumothorax, leading to inappropriate thoracocentesis or tube thoracostomy and inadvertent perforation of the herniated viscera [77]. Gastric, biliary, or intestinal contents or fecal smell confirms the diagnosis of DH with abdominal organs in the hernia sac.

In an unconscious, pale, and cyanosed patient, the blood pressure could be unrecordable with signs of a tension pneumothorax. It is a true emergency, and a surgeon performs needle thoracocentesis inserted via the second left intercostal space anteriorly or standard tube thoracostomy.

Chest drains in pregnancy should always be inserted using blunt dissection [92] after repositioning the abdominal viscera if possible.

### 20.5.1 Laboratory Findings

Serum laboratory findings and urinalysis are mostly normal except for WBC and oxygen saturation [83, 93–95]. Leukocytosis can be physiologic; a left shift is absent if the herniated organs are vital. Oxygen saturation can be lowered if a large mass of intra-abdominal organs is present

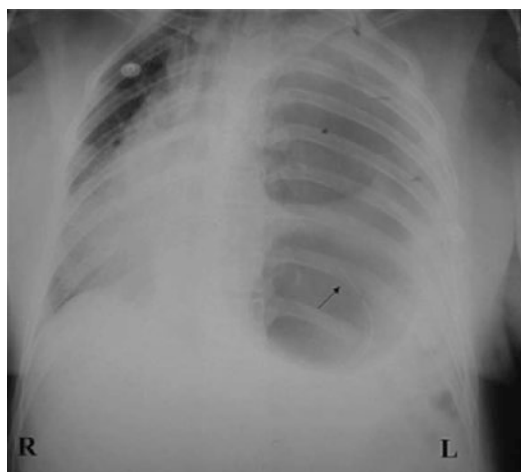
in the thorax, especially with the shift of the mediastinum.

## 20.5.2 Chest Radiography

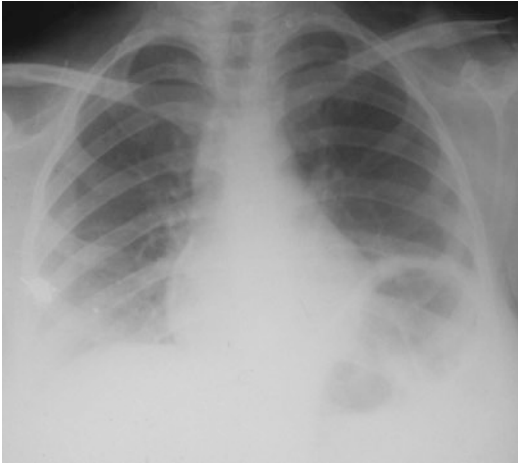
### 20.5.2.1 Plain Chest X-ray

The key to diagnosis in an elective or emergent setting is a chest radiograph which may show elevated diaphragm, pleural effusion [84] (Fig. 20.3), retrocardiac air in bowel lumen, air–liquid levels with hollow viscus obstruction (Fig. 20.4), nasogastric tube in the herniated stomach above the diaphragm, or mediastinal shift to the contralateral side due to compression (Fig. 20.5) [16, 96]. Sometimes, the right Morgagni hernia could be misinterpreted as a *Chilaiditi sign* (radiographic finding of bowel interposed between the liver and right hemidiaphragm), mostly treated conservatively [97]. The results are either diagnostic or abnormal and suggestive of diaphragmatic rupture in 75–97% of cases [96], although there are cases of initial pneumonia diagnosis later diagnosed as DH [25, 88].

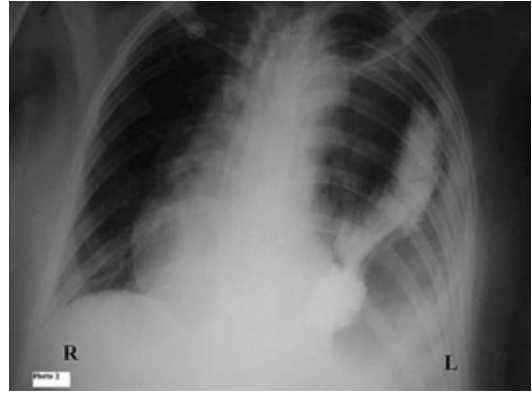
Chest X-ray of the diaphragmatic eventration can mimic DH, which is not an indication of the operation (Figs. 20.6 and 20.7).



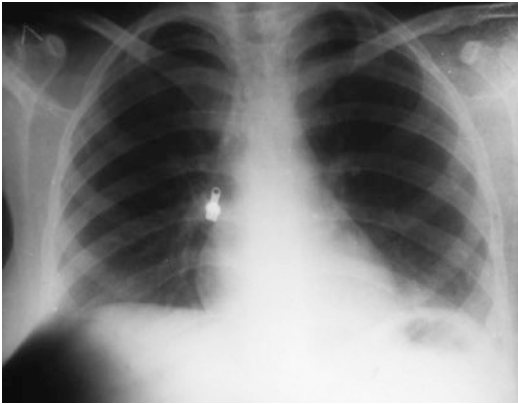
**Fig. 20.5** Chest radiograph shows a mediastinal shift to the right. In the left, hemithorax are two large bullae. The arrow indicates the nasogastric tube in the herniated stomach above the diaphragm. (Reproduced with permission from [16])



**Fig. 20.6** Left dome of the diaphragm is raised, lying above the level of the right dome, with its peak reaching up to the 7th posterior rib, suggesting eventration. (Reproduced with permission from [68] under the CC Attribution License)



**Fig. 20.8** Herniation of the stomach in the left hemithorax seen after postpartum gastrografin contrast administration. (Reproduced with permission from [16])



**Fig. 20.7** Post-delivery chest radiograph of the same patient as in Fig. 20.5 showing resolution of eventration of the diaphragm with the normal position of the left dome at the left posterior 8th rib. (Reproduced with permission from [68] under the CC Attribution License)

#### 20.5.2.2 Chest X-ray with Peroral Contrast

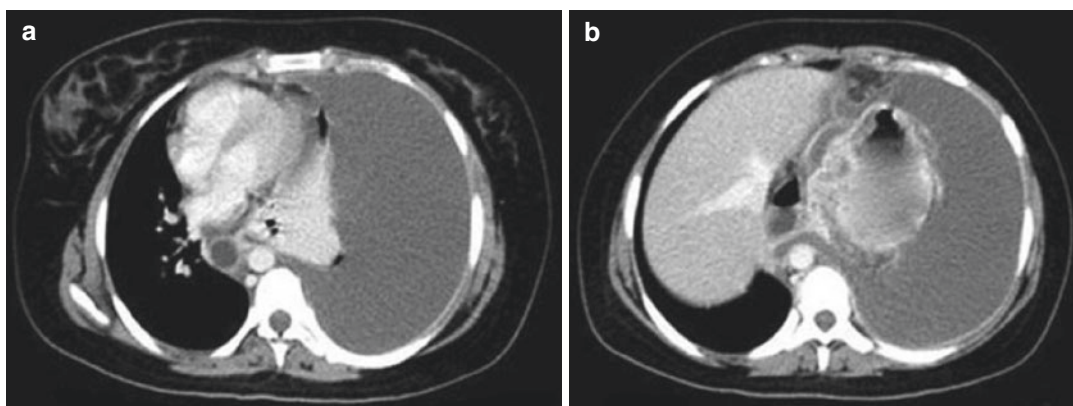
Clinical suspicion of DH without clear findings on plain chest X-ray indicates peroral barium contrast establishing the diagnosis when contrast-filled abdominal organs are located in the chest (Fig. 20.8). Contrast X-ray is more frequently used in the postpartum period. With esophageal rupture, oral contrast usually reveals a defect in the esophagus.

### 20.5.3 Thoracic Ultrasound

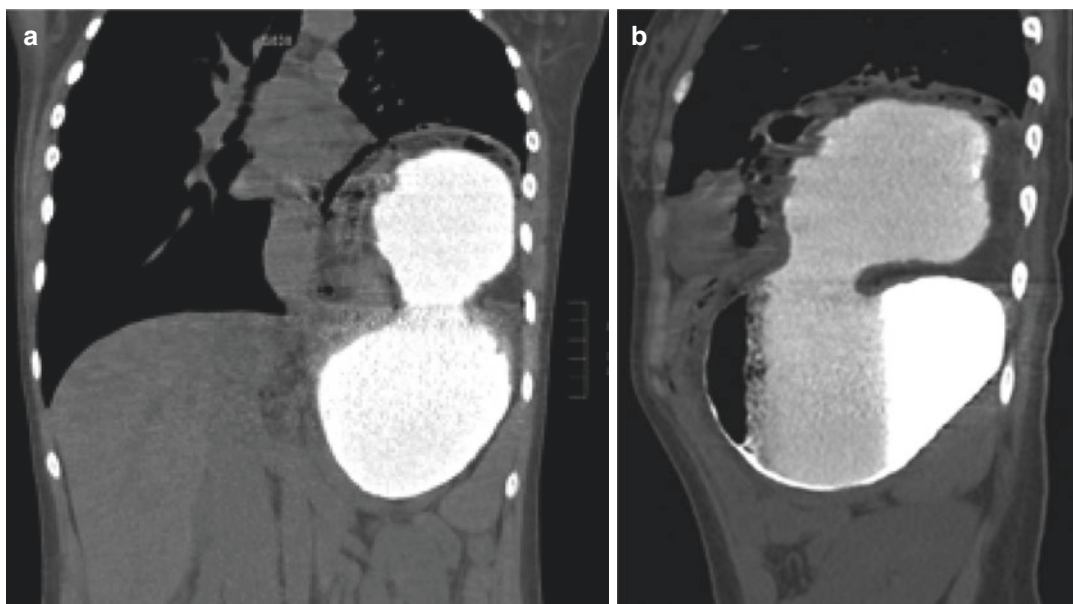
The thoracic US may define the integrity of the diaphragm, the content of eventration, and other diaphragmatic pathologies in the general population [98]. There are no studies on the pregnant population to diagnose maternal DH.

### 20.5.4 Thoracic CT

Suspected or proven DH clinically or on chest X-ray in a stable patient indicates CT of the thorax and abdomen with maternal pelvic lead shielding [88]. With suspected perforation, water-soluble peroral contrast detects the localization of the perforation. With perforation, pleural effusion will be evident (Fig. 20.9). Also, with partial obstruction/strangulation of the stomach, the typical hourglass (*the collar sign*) is visible (Fig. 20.10). Also, a *dependent viscera sign* means herniated viscera are falling to a dependent position against the posterior ribs with the patient in a supine position. Mediastinal shift results from a large volume of intra-abdominal organs within the thoracic cavity (Fig. 20.11). The stomach in the thoracic cavity causing a mediastinal shift is termed *tension gastrothorax* [76, 79].

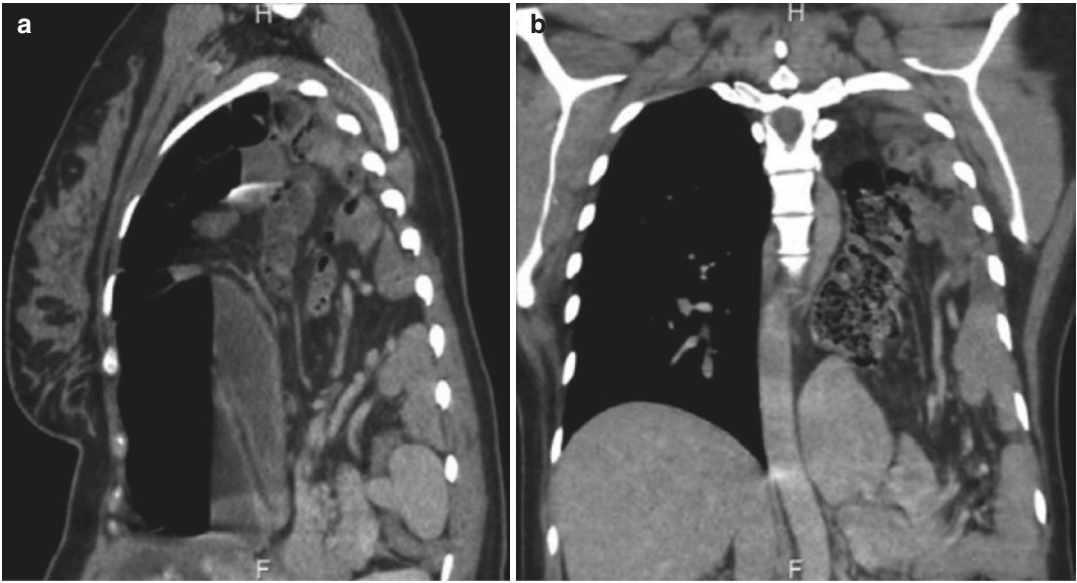


**Fig. 20.9** CT shows (a) a massive left pleural effusion associated with severe contralateral mediastinal shift and (b) a complete intrathoracic gastric herniation. (Reproduced with permission from [81])

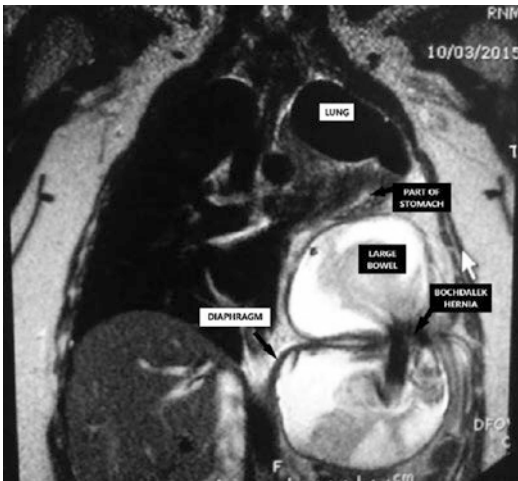


**Fig. 20.10** Front view (a) and lateral view (b) of the CT show the left diaphragmatic rupture and the typical aspect of the stomach in the form of the hourglass (*the collar sign*). (Reproduced with permission from [99])





**Fig. 20.11** A thoracic CT. (a) Sagittal and (b) coronal planes show the intrathoracic content of the large left Bochdalek's hernia resulting in the mediastinal shift. Abdominal lead shielding was used [88]



**Fig. 20.12** MRI shows a large left-sided Bochdalek's hernia. The sac contains parts of the stomach and colon. (Reproduced with permission from [34])

### 20.5.5 Thoracic MRI

Recently, thoracic MRI, with high sensitivity and specificity [61, 100], has been used for the diagnosis (Fig. 20.12) instead of thoracic CT. Image quality can be poor due to severe dyspnea [101].

## 20.6 Treatment

Elective laparoscopic repair should be considered in women of childbearing age with DH or eventration identified before pregnancy. This prevents diaphragmatic rupture and its associated risks during future pregnancies.

### 20.6.1 Conservative Treatment

Symptomatic DH without signs of complete hollow alimentary organ obstruction, visceral strangulation, or infarction can be treated conservatively initially.

**Nasogastric Suction** In preparation for the emergent operation, the treatment of nausea, vomiting, and abdominal distension by nasogastric suction is therapeutic because it decreases intra-abdominal, intragastric, and intrathoracic pressure. Also, it lessens mediastinal shift, improving oxygenation, especially when tension gastrothorax (herniation of the stomach with or without other intra-abdominal organs into the



chest) is the cause [95]. Therefore, it ameliorates symptoms, both gastrointestinal and respiratory [102]. Such improvement allows delayed surgery until transfer to a tertiary care center or allows full effect of antenatal corticosteroids (see Sect. 20.6.3) [61].

**Oxygen** Oxygenation is impaired when abdominal organs are in the thorax. Therefore, oxygen delivery in the perioperative period is mandatory.

**Intravenous Fluids** Due to excessive vomiting and nil by mouth, dehydration with electrolyte abnormalities is present. The intravenous fluid administration should start immediately after the clinical examination.

**Nutrition** One of the potential challenges of expectant management is achieving adequate nutrition in pregnancy. Malnutrition for prolonged periods can be associated with intrauterine growth restriction, increased perinatal morbidity and mortality, maternal weight loss, electrolyte imbalances, and vitamin deficiencies [103]. Total parenteral nutrition should be considered if the patient cannot tolerate oral or nasogastric feeds due to a likely partial obstruction from the large hernia. Some recommend CS with simultaneous DH repair or delayed laparoscopic repair after CS (see Sect. 20.6.2).

## 20.6.2 Surgical Treatment

### 20.6.2.1 Operative Indications

#### Before Pregnancy

Women with DH planning pregnancy should be operated on before pregnancy to eliminate the possibility of developing symptomatic or strangulated DH during pregnancy [24]. Cases of recurrent DH during pregnancy after a pre-pregnancy DH operation (see Sect. 20.7.1.2).

#### Asymptomatic Patients

For asymptomatic patients, some recommend CS after fetal lung maturity with simultaneous hernia

repair before the onset of labor. The recommendation is based upon maternal and fetal morbidity being 55% and 27%, respectively, when vaginal delivery was attempted before the DH repair [26]. The fact that most women had previous uneventful pregnancies with the DH opens the question of whether exposing an asymptomatic mother and fetus to the morbidity of antenatal repair [65]. Until 1935, only 12% of women with small and moderate degrees of paraesophageal DH during late pregnancy had the DH demonstrated radiologically in the postpartum period [22]. Though further stretching of the hiatus is possible during pregnancy and labor, the hernia will regress as soon as the increased intra-abdominal pressure is removed. The condition will often revert to normal with small and moderated DH. This is supported by the cessation of symptoms in nearly all cases after the puerperium. Therefore, others [61] recommend

*Vaginal delivery* with the following:

- Planned induction of labor (to avoid precipitous labor at a remote site),
- Regional anesthesia to help prevent the urge to bear down,
- The use of instrumentation to shorten the second stage of labor.

There are cases of symptomatic DH in previous pregnancies [65]. Due to severe and prolonged vomiting and weight loss or even hematemesis, there are cases of fetal loss. In such cases, elective repair prevents similar presentations in further pregnancies [67].

#### Symptomatic Patients

Symptomatic DH should be managed without delay because of the associated high maternal and fetal mortality rates if left uncorrected [26, 61, 62]. Even if the pregnancy is normal, puerperal symptomatology is possible. One recommends that if the diagnosis is made in the first trimester, then the patient should be carefully monitored and observed in the absence of complications. Surgery is delayed until the second

trimester when organogenesis is complete before the increasing bulk of the gravid uterus risks further herniation. Others suggest repair shortly after diagnosis, regardless of gestation, because the condition is associated with a poor or complicated outcome, particularly if early surgical intervention is not undertaken [26]. Others support conservative therapy when long-standing DH is present, even when symptomatic. In such circumstances, CS is performed after 30 weeks of pregnancy, and laparoscopic repair is deferred after the completion of breastfeeding [104].

### Emergent Presentation

Signs of visceral strangulation and infarction are surgical emergencies, indicating immediate operation, irrespective of fetal maturity. Strangulation and gangrene of the herniated viscera indicate segmental resection of the involved portion with the re-establishment of bowel continuity. The diaphragmatic defect should be closed with interrupted sutures. If the defect is large, then the mesh should be used. If the fetus is viable, then CS is recommended. With nonviable living fetuses, the pregnancy is allowed to continue. The timing and the route of delivery should be discussed with the obstetrician.

With an obstructive shock (tension pneumothorax, mediastinal shift, cardiac arrest), chest decompression is the priority. It is achieved by nasogastric suction, endoscopy, or intercostal drainage of the herniated organ [105].

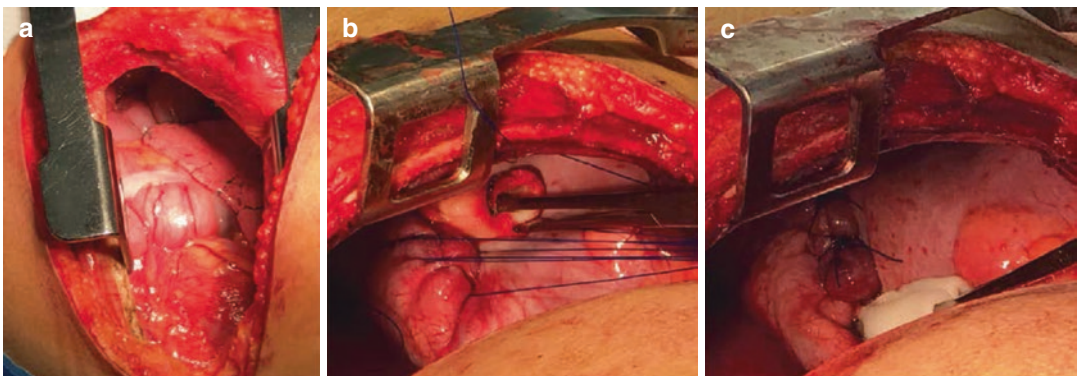
### 20.6.2.2 Open Surgery

#### Transthoracic Approach

The transthoracic approach is indicated for previously operated DH by the transabdominal approach due to dense intrathoracic adhesions [44, 106, 107].

Under normal circumstances, the best surgical approach is lateral thoracotomy at the level of the 7th or 8th rib [56] because it provides a better view of the diaphragm while it requires one-lung ventilation. If strangulation has occurred, the incision should be planned as a thoracoabdominal approach for adequate exposure and easier access to the bowel, particularly if the colon is involved. Also, a separate laparotomy can be done. Some prefer the transthoracic approach due to the limited intra-abdominal space from the gravid uterus [88]. Once the adhesions are separated, the diaphragm repair is easily achieved, and there is usually sufficient tissue to make a Mayo-type repair with nonabsorbable sutures (Fig. 20.13). If the tear destroys the musculature of the esophageal hiatus, then this should be carefully reconstituted. When the diaphragm is avulsed from the chest wall, with insufficient tissue left peripherally, repair should be affected by suturing the free edge to the chest wall with interrupted sutures to two adjacent intercostal muscles to obtain a wider adherence.

One opinion is that there is no justification for paralyzing the phrenic nerve, even by “temporary”



**Fig. 20.13** Intraoperative image shows (a) left thoracotomy wound with colon and small bowel content, (b) repair of the hernia defect with interrupted nonabsorbable

sutures, and (c) the repaired hernia defect. (Reproduced with permission from [88])

crushing. However, on rare occasions, subperiosteal resection of lower ribs may be necessary to close a peripheral tear. An underwater seal system should always drain the thoracic cavity. With intrathoracic perforation (Fig. 20.14a), a gastric ulcer due to NSAIDs could be found (Fig. 20.14b). A primary repair includes full-thickness interrupted sutures for closing the perforation. Then, after replacing the stomach within the abdominal cavity, direct double-layer closure of the DH defect is completed.

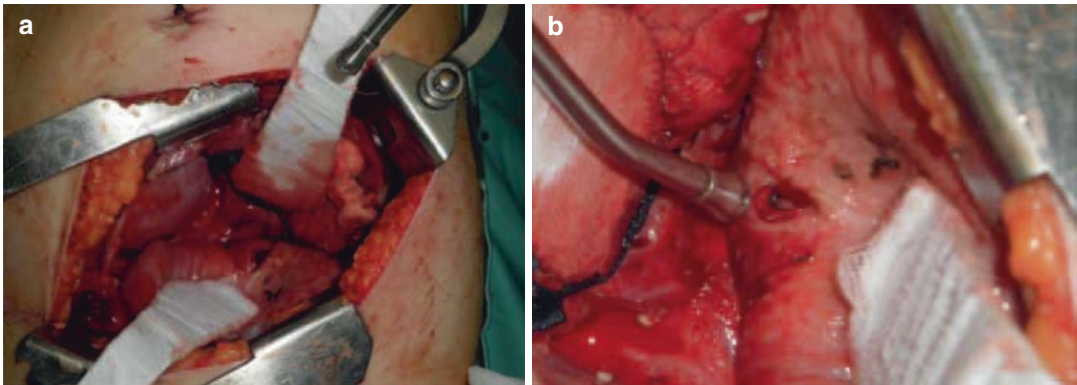
### Transabdominal Approach

The transabdominal approach enables good access to herniated parenchymal organs such as the liver and spleen [108], mobile cecum, and

anterior (Morgagni) DH (Fig. 20.15). The transabdominal approach is preferred because it is less invasive [109]. However, some prefer the trans-thoracic approach in longer-lasting hernias to treat pleuroperitoneal adhesions. On the other hand, the transabdominal approach is better in pregnancy if CS is indicated or other intra-abdominal pathologic findings should be resected, such as gangrenous bowel or gallbladder stones. Most explorations are through median laparotomy, although a subcostal incision can be performed [100].

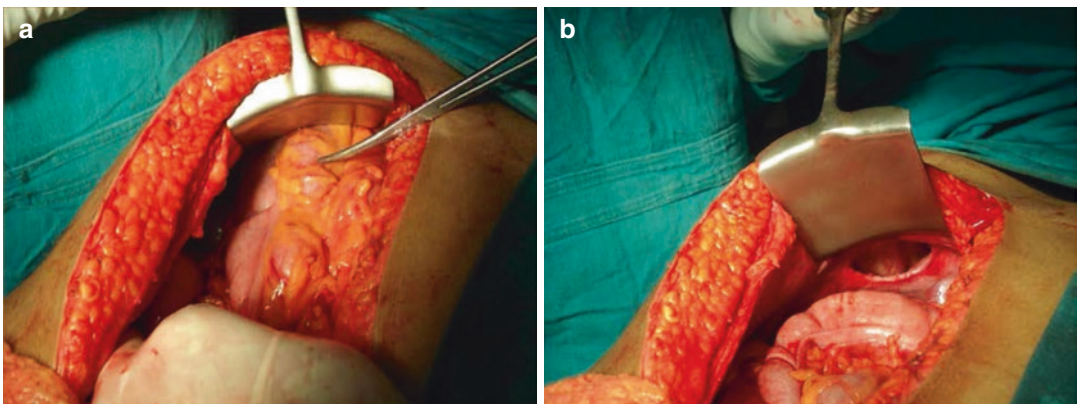
### Thoracoabdominal Approach

The extended approach is when the abdominal incision is extended into thoracotomy or vice



**Fig. 20.14** Findings during emergency thoracotomy. (a) Complete intrathoracic gastric herniation through a large diaphragmatic hiatal defect without macroscopic signs of

visceral strangulation, and (b) a well-defined 1 cm gastric ulcer at the lesser curvature. (Reproduced with permission from [81])

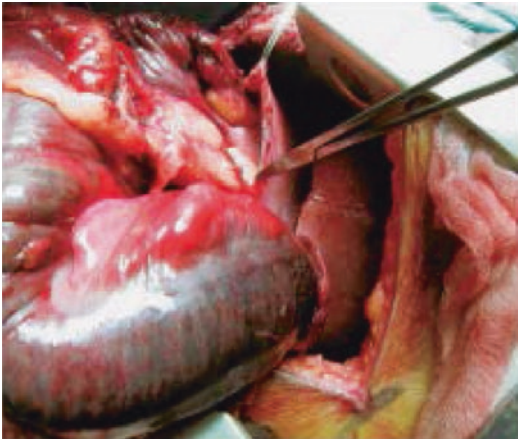


**Fig. 20.15** (a) Herniation of the vital transverse colon and omentum through (b) anterior (Morgagni) diaphragmatic defect (6 × 4 cm), 5 cm from the midline. (Reproduced with permission from [101])

versa. The abdominal incision is necessary if wide resections of gangrenous organs are needed (Fig. 20.16).

### 20.6.2.3 Laparoscopic Surgery

The laparoscopic approach is safe, feasible, and efficacious in nonpregnant patients [111]. However, some technical difficulties in pregnant women might discourage surgeons from using this approach. However, the laparoscopic approach and repair during pregnancy are increasingly used [11, 93, 112–117]. Avoiding laparotomy eliminates the possibility of abdominal wall disruption during and after delivery and postoperative hernia. The disadvantage is that CS should be performed through a separate incision.



**Fig. 20.16** Bochdalek's hernia in the left hemidiaphragm with the gangrene of a large part of the herniated gangrenous transverse colon. (Reproduced with permission from [110])

**Fig. 20.17** Frank right lateral decubitus with fetal monitoring during laparoscopic left diaphragmatic hernia (Bochdalek-type) repair [117]



Simultaneous Pfannenstiel incision for CS, after the laparoscopic procedure is completed, results in excellent cosmetic results. Also, the laparoscopic operation can be done after vaginal delivery [11, 116] or CS [118] as a secondary procedure.

### Supine Position

The abdomen is entered through a midline epigastric incision. Hasson's open technique enables trocar placement under direct visualization [93]. Another option is the Veress needle insertion in the left hypochondriac region [113]. After insufflation of 12 mmHg, the laparoscope is introduced through a 10 mm port placed halfway between the umbilicus and the xiphoid process, revealing the abdominal contents. The patient is positioned in a steep reverse Trendelenburg, and four additional 5-mm (or 3 with one 10 mm) ports in the left and right hypochondrial area are placed under direct visualization [93].

### Lateral Position

The patient is positioned in frank right lateral decubitus with double-lumen endotracheal intubation. An electronic fetal monitoring device is positioned on the right lower part of the abdomen (Fig. 20.17). An initial 12-mm port is inserted using an open technique, 2 cm below the left costal margin on the anterior axillary line. The pneumoperitoneum pressure is limited to 12 mmHg during the procedure. Three 5-mm ports and another 12-mm port are inserted under direct vision below the left costal margin. A 10-mm 30-degree laparo-



scope is used. The DH with hernia contents is identified. The contents are reduced using gravity and atraumatic graspers and inspected for viability. Adhesions between the omentum and the left lower lobe of the lung are dissected with a monopolar cautery hook. The posterior and lateral chest wall insertions of the diaphragm could be mobilized to facilitate the approximation of the lateral borders of the diaphragm.

Although rarely used [117], the lateral position has many advantages over the supine position. First, it permits a complete view of the diaphragm, the subdiaphragmatic space, and the thorax. In this position, gravity helps to retract the spleen, the stomach, and the uterus without manipulation. This reduces the risk of iatrogenic injury, especially to the gravid uterus. Also, a thoracoscopy could be easily accomplished without any repositioning. Right lateral tilt is usually discouraged during pregnancy because of inferior vena cava compression risk. Therefore, a more pronounced frank right lateral decubitus reduces inferior vena cava compression by a posterolateral uterine displacement. This position could be tried preoperatively with fetal and maternal monitoring for 1 h to ensure maternal hemodynamic stability and fetal well-being [117].

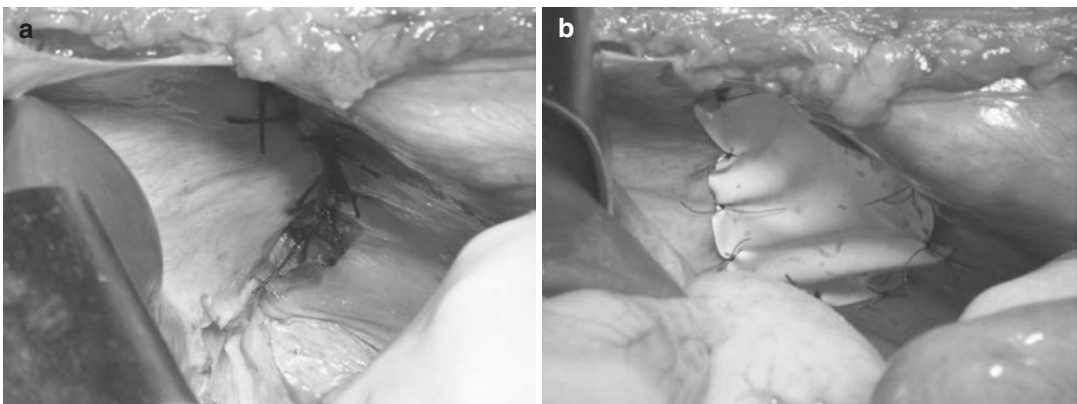
#### 20.6.2.4 Diaphragmatic Defect Closure

The best method of closure of the diaphragmatic defect in the general population is still unclear.

Primary repair is done for most defects unless these are large (Fig. 20.18a). When the edges can be easily opposed, primary closure with nonabsorbable sutures in a single layer is preferred. If the defect is large and under tension, then a prosthetic patch [100] is recommended (Fig. 20.18b).

Some authors use Marlex mesh to close wide diaphragmatic holes and then cover the defect with a pedunculated flap, using the falciform ligament or the peritoneum. Gore-Tex mesh can be covered with the falciform ligament to close a large diaphragmatic gap. Two different surfaces characterize the polytetrafluoroethylene patch: one that promotes fibrous ingrowth into the patch and another relatively resistant to adhesion formation placed adjacent to the abdominal viscera. Generally, a prosthetic patch should not be used if intestinal strangulation has occurred because of a risk of postoperative (mesh) infection. In clean-contaminated and contaminated conditions, wound and mesh-related infections occurred in 7–21% of patients in the general population but did not usually require mesh excision [120]. Some authors advocate placing a prosthetic patch for abdominal wall reconstruction in clean-contaminated conditions [121]. The third option is direct closure with sutures with the addition of a mesh [74].

With a small number of cases in pregnancy (less than 100), specific indications for different procedures are not defined. Therefore, it is recommended to perform the procedure indicated in



**Fig. 20.18** (a) Completed hernia repair. A hernia was repaired with interrupted sutures. (b) The final appearance of the repair with the Gore-Tex sheet (Gore Preclude Dura substitute). (Reproduced with permission from [119])



the general population, especially in the subsets of patients with similar intra-abdominal pressure dynamics: (1) repair after CS at the same operation or (2) during the postpartum period.

### 20.6.2.5 Abdominal Organ Operations

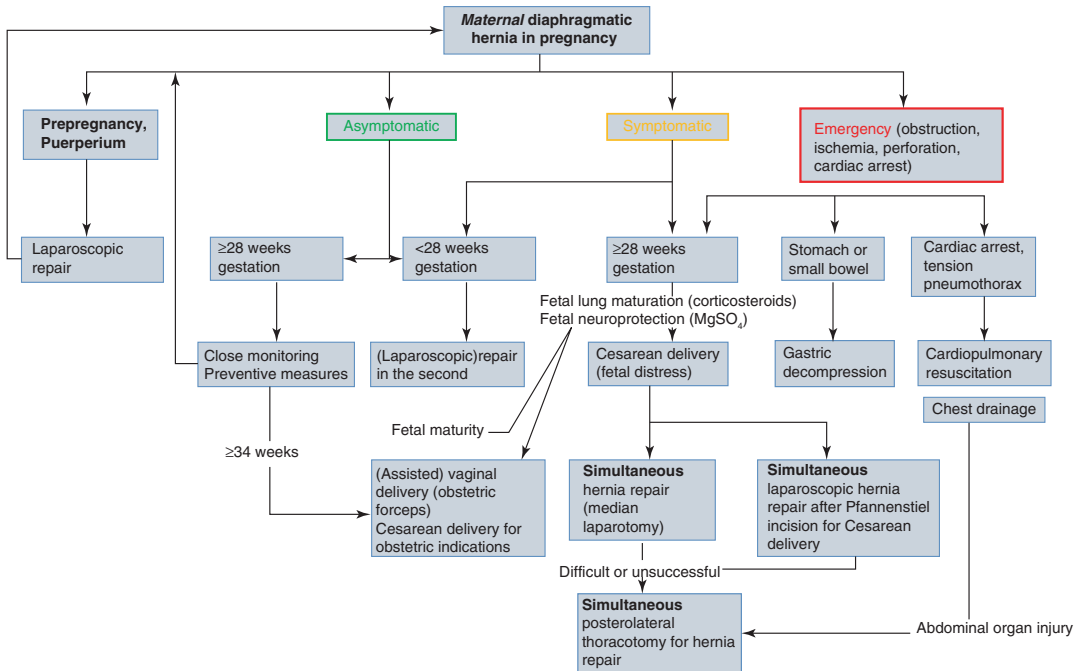
Most principles are the same as in the nonpregnant population. Also, most principles are the same for pathologic conditions in the thorax instead of the peritoneal cavity. The question arises when an obstruction or perforation of the ascending or transverse colon occurs. It can be caused by distension, strangulation, or iatrogenic perforation with needle thoracocentesis or tube thoracostomy. Fecal spillage in the thorax does not cause peritonitis. It is not scientifically evaluated whether anastomosis of these segments can be performed in the “native” peritoneal cavity without contamination [77].

### 20.6.3 Obstetric Management

The indication for the delivery and mode of delivery is trimester dependent. If a hernia mani-

festes in the third trimester, once fetal maturity is documented, then the baby should be delivered by CS with simultaneous repair of a DH [26, 65, 122]. Standard vaginal delivery should be avoided because an increase in intra-abdominal pressure may further displace the viscera and result in strangulation of the herniated viscus or disruption of DH repair. On the contrary, others state that uterine contractions, unlike the Valsalva maneuver, do not increase intra-abdominal pressure and are unlikely to cause rupture at the repaired site. Thus, a patient with a repaired DH can labor and deliver vaginally [61]. The labor cannot be completed without contractions of abdominal wall musculature and the Valsalva maneuver. Therefore, it is safer to perform CS. During vaginal delivery, obstetric forceps and a vacuum extractor can be applied during the second stage of labor to prevent the patient from bearing down, minimizing the increase in intra-abdominal pressure [61]. The proposed therapeutic algorithm is presented in Fig. 20.19.

Corticosteroids for fetal maturity should be administered to the mother before surgery when the gestational age is between 24 and 34



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**Fig. 20.19** A proposed therapeutic algorithm for a diaphragmatic hernia during pregnancy [123]

weeks because of the risk of preterm delivery during or after surgery. The patients who had undergone DH repair during their first or second trimester are allowed to deliver vaginally. Uterine contractions do not increase intra-abdominal pressure and are unlikely to cause rupture at the repair site [61]. Approximately 23% presented after 24 weeks of pregnancy and delivered vaginally. Three of these cases were in the context of preterm labor or fetal death in utero [25].

## 20.7 Prognosis

### 20.7.1 Maternal Outcome

#### 20.7.1.1 Maternal Mortality

Maternal mortality depends on the following:

- Type of presentation,
- Type of DH,
- Duration of symptoms,
- Mediastinal shift,
- Strangulation with/without perforation.

It is difficult to claim the maternal mortality rate due to a difference in inclusion criteria. There was a wide range of maternal mortality from complicated DH in pregnancy during the first half of the twentieth century, from 7.7% [124] to 58.3% [80]. In that period, 31 symptomatic patients without further complications were treated conservatively without maternal mortality [125]. The main life-threatening complications were acute respiratory distress caused by compression atelectasis, mediastinal shift, strangulation, and gangrene of the herniated viscera [11, 26, 33, 44, 57, 80]. Therefore, the leading causes of maternal death are hypoxia and acidosis. In these cases, the maternal mortality rate ranges from 42–58.3% [26, 45, 80, 126, 127]. The current maternal mortality rate is 10–11% [24, 25]. Cardiac arrest results in maternal mortality of 33% [65, 75, 76, 85, 105, 128].

#### 20.7.1.2 Recurrent Diaphragmatic Hernia

The recurrence rate of DH following repair in the general population depends on the severity of the original defect and the type of repair. About half of the prosthetic patch repairs of CDH were reherniated and required revision within 3 years [129]. Several cases had DH repair before pregnancy [24, 34].

The prepregnancy repair is a risk factor for (recurrent) DH during pregnancy [34]. The risk of a recurrent DH exists after the repair during pregnancy, labor, or puerperium.

### 20.7.2 Fetal Outcome

Fetal mortality and morbidity result from premature labor and compromise maternal oxygen delivery [130]. The complication rates are more frequent in the third trimester of pregnancy—up to 1988, fetal deaths occurred in 50% of cases and premature birth in 24% [26]. In 30% of the reported cases, delivery was by CS [65]. Recent literature reviews claim an overall fetal mortality rate of 13–19% [24, 25]. Patients presenting with cardiac arrest due to DH have a fetal mortality rate of 50% [65, 75, 76, 85, 105, 128].

Maternal CDH could increase the risk of newborn CDH [65]. Familial CDH is inherited through an autosomal recessive pattern but is responsible for only 2% of CDH [131].

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## Abstract

The incidence of inflammatory bowel disease is rising in the general population. Consequently, it is increasing in the pregnant population. The severity and progression of the disease depend on the disease activity during pregnancy. Therefore, achieving remission before a planned pregnancy is mandatory, minimizing the possibility of disease progression and complications during pregnancy. When inflammatory bowel disease during pregnancy is active, some immunomodulators and biological agents can influence fetal development. On the other hand, a prolonged course of active disease during pregnancy increases the rate of preterm labor, fetus small for gestational age, and other obstetric complications. An additional problem is pouch surgery before and during pregnancy because functional results can be lower due to the compression of the growing uterus. Also, the type of delivery could be influenced by the pouch surgery and ileal pouch-anal anastomosis function at the time of delivery. Previously avoided, now recommended, vaginal delivery with a pouch does not adversely affect the pouch function.

## 21.1 Crohn's Disease

### 21.1.1 Historical Perspective and Incidence

German surgeon Wilhelm Fabry (Fig. 10.1), also known as William Fabry, Guilelmus Fabricius Hildanus, or Fabricius von Hilden, first observed Crohn's disease (CD) in 1623 [1]. The disease was later described and named after the US physician Burrill Bernard Crohn [2]. In the general population, CD incidence in Western countries increased markedly between the 1950s and the 1980s [3, 4]. Since the 1980s, the incidence has increased at a slower rate [5, 6]. Nowadays, the highest incidence is in North America (20/100,000) and Australia (16–17/100,000), followed by Western Europe (9–13/100,000). The incidence is lower in the Middle East and other Asian countries (0.2–5/100,000). The incidence of inflammatory bowel disease (IBD) has a bimodal distribution curve with a higher peak in younger patients: 50% of patients are younger than 35 years at the time of diagnosis [7], and 25% conceive for the first time after their diagnosis of IBD [7–9]. This age range corresponds to the female reproductive age and increases the likelihood of CD during pregnancy.

Williams W. Babson first described intestinal obstruction (with the abscess from ileocolic disease) from CD during pregnancy in 1946 [10]. Approximately 40 pregnant patients with surgical management of complicated CD were described [11–13]. The median age at the surgery was 24.5 [14–30] years. Almost half presented in the second trimester, and half of all cases were diagnosed during pregnancy [12].

### 21.1.2 Effect of Pregnancy

The interaction between CD and pregnancy is bidirectional: CD impacts pregnancy, and pregnancy may impact CD.

#### 21.1.2.1 Modulatory Effects of Pregnancy on Inflammatory Bowel Disease

The maternal immune system is modified during pregnancy. A possible factor inducing quiescent disease may be a disparity in HLA class II antigens between mother and fetus, suggesting that the maternal immune response to paternal HLA antigens may result in immunosuppression that affects the maternal immune-mediated disease. This has been demonstrated in IBD also [31]. Increased laxity of fibrous tissues, partly due to the hormone relaxin, an insulin-like peptide produced by the corpus luteum, results in dissolved and disorganized collagen fibers [32]. Serum pro-inflammatory cytokines (IL-6, IL-8, IL-12, IL-17, and TNF- $\alpha$ ) decrease significantly during conception in patients with IBD [33]. Epithelial paracellular permeability decreases during the estrogen-dominant phase of the cycle compared to the progesterone-dominant phase, consistent with improved barrier integrity in response to elevated estrogen levels in pregnancy [34]. The intestinal microbiome diversity of patients with IBD normalizes during middle and late pregnancy [33]. These pregnancy-induced effects on the immune system (Table 21.1) and fibrous tissue could affect the bowel in CD: reducing the chronic inflammatory response, fibrous tissue formation, and the frequency of stenosis and

resection rates [31, 35]. The increasing parity reduces the need for further surgical resections, confirming this immunoprotective role of pregnancy [36].

The diagnosis during pregnancy is a favorable prognostic indicator in distal ileal and colonic CD. Also, multiple perioperative blood transfusions may decrease recurrence in CD by decreasing immune responsiveness [37].

#### 21.1.2.2 Disease Activity During Pregnancy

Crohn et al. in 1956 suggested that if the onset of the disease occurs during pregnancy, its subsequent course is severe and relapsing [15]. This was challenged by suggesting that CD activity is unaffected by pregnancy [16] and that CD activity during pregnancy reflects the disease activity at the time of conception [17]. Measurement of CD activity, however, as a single-point assessment of a lifelong disease is an incomplete measure of long-term outcomes. Abramson et al., in 1951, classified pregnant patients with CD (originally idiopathic ulcerative colitis) into four categories [18]:

- Category I—inactive at conception,
- Category II—active at conception,
- Category III—arising during gestation,
- Category IV—arising during the puerperium.

Several factors are responsible for the higher remission rate and lower disease activity (Harvey–Bradshaw index) during pregnancy [19, 33]. The first factor is the increased steroid production during pregnancy and the fall off during the puerperium. The amelioration of symptoms followed by relapse during the puerperium would thus be the natural consequence. Approximately 25% have worsening CD activity postpartum [20]. The second factor is that a Th<sub>2</sub> shift during pregnancy ameliorates disease in those patients in whom Th<sub>1</sub> responses dominate (such as CD) while aggravating disease in Th<sub>2</sub>-dominant patients (mainly UC). The third factor is a

**Table 21.1** Changes in the immune system during pregnancy and IBD

|                                              | Cell type                    | Subtype                                                                                                        | Function                                                                                                                                                                                                                        | Changes in IBD                                                                                                  | Changes during pregnancy                                                                                                                          | Conceivable effect of changes during pregnancy on IBD                             |
|----------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| Epithelial barrier                           | Goblet cells<br>Paneth cells |                                                                                                                | Production of a mucous layer<br>Release of antimicrobial peptides                                                                                                                                                               | Decrease of mucus layer in IBD<br>Decrease of antimicrobial peptides in IBD                                     | Improved barrier integrity in response to estrogen                                                                                                | Positive effective, mainly due to increased estrogen                              |
| Innate immune system; adaptive immune system | Monocytes                    | Macrophages and dendritic cells (DCs)                                                                          | Phagocytosis and digestion of pathogens<br>Antigen presentation and activation of the adaptive immune system<br>DCs express IDO1, which induces apoptosis of CD8+ T cells and promotes differentiation of CD4+ T cells to Tregs | Increased in IBD<br>Skewing of macrophages from M2 (important for wound healing) to M1 (inflammatory) phenotype | Decrease from early pregnancy to mid-gestation<br>Skewing toward M2 wound healing macrophages at placental interface<br>Fetal tolerance via Tregs | Positive effects through circulating M2 macrophages and Tregs and their cytokines |
|                                              |                              |                                                                                                                | Phagocytosis and digestion of pathogens<br>Release a number of different effector molecules at site of infection                                                                                                                | Increased in IBD                                                                                                | Decrease from early pregnancy to mid-gestation                                                                                                    | Decrease during pregnancy may have a positive effect on IBD course                |
|                                              | Natural killer (NK) cells    |                                                                                                                | Secret cytokines such as IFN- $\gamma$ and TNF- $\alpha$ , which act on macrophages and DCs<br>Ability to kill tumor cells without any priming or prior activation                                                              | Increased in CD                                                                                                 | Increase of placental and decidual NK cells                                                                                                       | Local effect during pregnancy, so probably no influence on the course of IBD      |
|                                              | Innate lymphoid cells (ILCs) | ILC1 (IFN- $\gamma$ , TNF- $\alpha$ )<br>ILC2 (IL-4, IL-5, IL-9, IL-13)<br>ILC3 (IL-17, IL-22, TNF- $\alpha$ ) | Secrete immunoregulatory cytokines                                                                                                                                                                                              | ILC1 increased in CD<br>ILC2 increased in IBD<br>ILC3 increased in IBD                                          | First trimester: Increase of ILC1 and ILC3                                                                                                        | Negative effect on CD, potentially beneficial effect on UC                        |

(continued)

**Table 21.1** continued

|          | Cell type    | Subtype                                                                                                                                                                                                                                                                                                                                                                                          | Function                                                                                                                                                                                                                                                              | Changes in IBD                                         | Changes during pregnancy                                                                                                                | Conceivable effect of changes during pregnancy on IBD                                                              |
|----------|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| Hormones | T cells      | T-helper 1 (Th1) ( <i>IL-2</i> , <i>IL-12</i> , <i>IFN-<math>\gamma</math></i> , <i>TNF-<math>\alpha</math></i> )<br>T-helper 2 (Th2) ( <i>IL-4</i> , <i>IL-5</i> , <i>IL-6</i> , <i>IL-9</i> , <i>IL-10</i> , <i>IL-13</i> )<br>T-helper 17 (Th17) ( <i>IL-17</i> , <i>IL-21</i> , <i>IL-22</i> )<br>Regulatory T cells (Tregs) ( <i>TGF-<math>\beta</math></i> , <i>IL-35</i> , <i>IL-10</i> ) | Cytotoxicity, antitumor and antiviral responses<br>Antibody mediated immunity by stimulating B cells<br>Protect cell surfaces by removing extracellular bacteria<br>Regulate the function of other T-cell subsets and thereby repress inflammatory processes          | Increased in CD<br>Increased in UC<br>Increased in IBD | First trimester:<br>Increased in local tissue<br>Second/third trimester:<br>Increased in local tissue<br>Second trimester:<br>Increased | UC more likely to flare during pregnancy<br>CD, not UC, may benefit from the shift to Th2 phenotype<br><br>Unclear |
|          | HCG          |                                                                                                                                                                                                                                                                                                                                                                                                  | Mediates early expansion of Tregs<br>Modulates DC responses by inducing IDO1 expression<br>Reduces inflammatory cytokines such as IL-17 while increasing IL-10 levels in vitro, hCG is able to stimulate peripheral blood DC subsets to maintain a tolerant phenotype |                                                        | Increase in first trimester                                                                                                             | HCG or its peptides may contribute to the amelioration of inflammatory processes                                   |
|          | Progesterone |                                                                                                                                                                                                                                                                                                                                                                                                  | Decrease of proinflammatory mediators (i.e., <i>TNF-<math>\alpha</math></i> , <i>IL-6</i> , <i>IL-1<math>\beta</math></i> , <i>NO</i> )<br>Increases IL-10 production by macrophages and monocytes                                                                    |                                                        | Increased during pregnancy, with a decrease before labor                                                                                | Conflicting data                                                                                                   |
|          | Estrogen     |                                                                                                                                                                                                                                                                                                                                                                                                  | Decreases inflammatory cytokine production (i.e., <i>TNF-<math>\alpha</math></i> and <i>IFN-<math>\gamma</math></i> )<br>Inhibits NO synthase activity<br>Decreases the recruitment of inflammatory cells                                                             |                                                        | Increased during pregnancy                                                                                                              | Conflicting data in animal studies and human studies regarding contraceptive use                                   |



|                |                                |  |                                                                                 |                                                                                                                                                                                                                                                                                                 |                                                                                                        |                                                                                                                            |
|----------------|--------------------------------|--|---------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Microbiome     | Bacteria and their metabolites |  |                                                                                 | Reduced diversity of the bacteria present<br>Decrease of anti-inflammatory <i>Firmicutes</i> (i.e., <i>Faecalibacterium prausnitzii</i> )<br>Increase of proteobacteria and Bacteroidetes phylum members<br>CD show a less stable microbiome and reduced diversity compared to patients with UC | Third trimester: Dysbiosis, resembling a state of low-grade inflammation of the gastrointestinal tract | Worsening of IBD because of increase of dysbiotic changes seen in IBD during pregnancy                                     |
| Microchimerism | Immune cells, stem cells       |  | Coexistence of two genetically different populations of cells in one individual | Maternal microchimerism is not increased in patients with IBD<br>Fetal microchimerism in IBD pregnancy remains to be investigated                                                                                                                                                               | Whole cells cross the placenta from mother to child and vice versa                                     | Fetal microchimerism in IBD pregnancy remains to be investigated, but adverse effects speculated in (auto) immune diseases |

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CD Crohn's disease, HCG human chorionic gonadotropin, IBD inflammatory bowel disease, INF interferon gamma, TNF- $\alpha$  tumor necrosis factor alpha, UC ulcerative colitis

gonadotropin-releasing hormone (GnRH) that acts as an intestinal motility inhibitor and myenteric plexus degeneration inducer. In pregnancy, the placenta secretes GnRH-like hormones. The GnRH receptors may be scattered differently throughout the small vs. large bowel. The motility effect may also be more significant in the small than large bowel [21, 22]. The fourth factor for reduced disease activity in pregnancy is reduced tobacco smoking [23]. Smoking decreases CD activity [19]. Although insignificant, a higher incidence of smokers among pregnant IBD patients is in the quiescent phase (43%) than in normal pregnant women (14%) [24]. The fifth factor is low estrogen increasing CD activity without an effect on UC; pregnancy is a high-estrogen state and may inhibit CD activity, whereas UC shows its “natural history” without being influenced by the hormonal pregnancy milieu [25].

Approximately one-third of women with inactive IBD at conception will relapse during pregnancy [24, 26–28], mostly in the first trimester [29], often due to discontinuation of maintenance therapy [30]. This risk of a flare (19–26%) is no greater than any other year of the patient’s life [38–41]. The only significant risk factor for disease relapse is a longer disease duration [38]. There are comparable postpartum flare rates in breastfeeding (26%) vs. not breastfeeding (29.4%) in IBD mothers [42]. Discontinuation of therapy while breastfeeding could be one of the determinants of the higher flare rate [43]. Currently, 80% of CD women in remission at conception remain in remission during pregnancy [38].

If conception occurs when IBD is active, 60–70% continue to have the active disease during the pregnancy despite medical therapy [38, 44–46]. One-quarter of patients with active IBD during pregnancy will experience chronically active disease; in about half of these patients, the disease will worsen (45% UC, 33% CD) [44]. The active disease has been associated with miscarriage, stillbirth, prematurity, and low birth weight (LBW) [45]. Thus, conception is advised when IBD is in remission. There is a decrease in relapse rate in CD patients 4 years after preg-

nancy compared to the 3 years before pregnancy [46]. The rates of CD relapse decreased in the years following pregnancy compared to prepregnancy (0.76 vs. 0.12 flares/year) [47]. Disease progression within 2 years after childbirth is significantly more frequent in those patients with active luminal disease than in women with inactive luminal disease before pregnancy. This was independent of the mode of childbirth [26]. Patients with CD, pregnant during their disease, did not have higher stenosis (37% vs. 52%) or resection (52% vs. 66%) rates.

Patients with IBD onset of the first episode during pregnancy comprise 13% of all pregnancies. Most are diagnosed during the first trimester; however, no significant association was noticed between the gestational age at diagnosis and clinical characteristics or outcomes [48]. Interestingly, 71% had UC [38, 48], although a small percentage in non-first episode UC patients may reflect a referral bias, as mild UC patients may not have been referred to tertiary centers. UC, as the first onset during pregnancy, may be easier to diagnose due to its unique presentation, that is, rectal bleeding, as opposed to CD during pregnancy, which comprises fewer specific symptoms—abdominal pain, diarrhea, and weight loss. More so, performing an unsedated flexible sigmoidoscopy for UC diagnosis is significantly easier than a total ileocolonoscopy, needed to diagnose CD. In the first episode of IBD during pregnancy, L1 Montreal classification for CD and E1 presentation for UC was significantly more common. More so, no cases of colonic CD were noted [48]. These findings suggest that colonic IBD may present a unique disease subtype. The least common are severe acute manifestations that require surgery [15, 49–51].

Prior CD-related surgery and biologic therapy are independent protective factors against relapse during pregnancy among women with quiescent disease at conception [52].

Classification

All patients should have their disease phenotype classified under the *revised Montreal Classification* (Table 21.2). Classification attempts to characterize the clinical patterns of CD [53, 54]. Also, it adds to a better understanding of the disease dynamics during pregnancy, treatment options comparison, and prognosis.

21.1.2.3 Pregnancy and Surgical Therapy for CD

Parity (before and after the diagnosis of CD) and surgical resections are associated with distal ileal and colonic CD [36]. Increasing parity reduces the need for further surgical resections. This trend is present even in patients who became pregnant after CD diagnosis. Results might be explained by severely ill patients with CD having impaired fertility or no desire for children at that time. Even patients who had been pregnant by the time of diagnosis of their CD need fewer surgical resections subsequently. The number of resections/patients is lower in the parous patients. Pregnancy at the time of CD diagnosis is associated with a longer interval between the first and second resection. A larger proportion of patients in the parous groups had either no or only one resection than those in the resection group. The differences could reflect changing surgical practice for almost four decades [36].

**Table 21.2** Definition of Crohn's disease phenotype according to the Montreal classification

| Age of onset     | Location                                    | Behavior                              |
|------------------|---------------------------------------------|---------------------------------------|
| 16 years (A1)    | Ileal (L1)                                  | Non-stricturing, non-penetrating (B1) |
| 17–40 years (A2) | Colonic (L2)                                | Stricturing (B2)                      |
| >40 years (A3)   | Ileo-colonic (L3)                           | Penetrating (B3)                      |
|                  | Isolated upper GI disease (L4) <sup>a</sup> | + “p” if perianal disease             |

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<sup>a</sup> L4 is a modifier that can be added to L1–L3 when concomitant upper gastrointestinal (GI) disease is present

21.1.3 Pathophysiology

21.1.3.1 Free Intestinal Perforation

Several possible mechanisms may account for the free perforation of CD during pregnancy. Either an abscess adjacent to the CD's segment ruptures by the mechanical stress of labor or the intra-abdominal viscera fails to wall-off inflamed segments. In the latter case, the large uterus may prevent the greater omentum and other abdominal contents from adequately localizing the inflammation (see Chap. 1). The avulsion of the ileal wall by the rapid retraction of the uterus in the postpartum period could lead to ileal perforation in the case of exacerbation of CD in pregnancy [55]. This should be considered when dosing postpartum uterotonics in these patients. The confirmation could be that the most common indication for CD surgery during pregnancy is small bowel perforation [12].

21.1.4 Clinical Presentation

21.1.4.1 Elective Presentation

Most patients have symptoms and diagnoses of CD before pregnancy. Diagnosis of new-onset CD in pregnancy is challenging. It requires a high degree of suspicion because the symptoms are often nonspecific and similar to normal pregnancy or hyperemesis gravidarum. CD symptoms depend on (1) the disease location in the digestive tract and (2) the severity. The most common CD symptoms in pregnant and nonpregnant women are diarrhea, whether bloody or non-bloody, abdominal pain, fever, feeling of a mass or fullness in the right lower abdomen, and weakness. Pregnant women often present insufficient weight gain related to malabsorption or decreased intake since patients with obstructing bowel segments feel better when they do not eat.

Physical examination may be normal or show nonspecific signs (pallor, weight loss). Also, extraintestinal manifestations of IBD should be searched

for (see Sect. 21.2.5.1). Proctologic conditions such as anal fissure, perianal fistula, and abscess are particularly associated with CD. Glossitis and aphthous ulcers in the mouth, beaking, or frank clubbing of the nails are common.

#### 21.1.4.2 Emergent Presentation

##### Intestinal Perforation

Free intestinal perforation presents as acute abdominal pain with signs of peritonism. The clinical presentation can defer depending on the pathophysiologic mechanism responsible for the perforation. If perforation due to obstruction is the cause, intestinal obstruction (see next paragraph) presents before peritonitis. Perforation due to progressive inflammation of the bowel wall results in abdominal pain of lesser intensity with possible mucus and diarrhea (with or without blood) that precede signs of peritonitis.

##### Intestinal Obstruction

In the early stages, the leading symptoms are abdominal distension, nausea, vomiting, and crampy abdominal pain. This initial phase can be accompanied by diarrhea and fever, sometimes misleading to gastroenterocolitis. This symptomatology can be present earlier or even before pregnancy [10]. With the progression, pain is constant, with no passage of stool or flatus. Also, CD patients are prone to partial bowel obstruction when the crampy abdominal pain or vomiting is related to larger meals or even every meal.

##### Intestinal Stomal Obstruction

See Sect. 18.7.

##### Presentation Mimicking Acute Appendicitis

The right lower quadrant pain mimics acute appendicitis (see Sect. 15.5). It is important to note symptoms before this acute presentation in the form of previous episodes of (crampy) abdominal pain, diarrhea, or loss of weight, which were not present if this is the first attack of the CD. Clinical differentiation is sometimes difficult in the general population, while pregnancy challenges the diagnostic process.

##### Obstetric Emergencies

Sometimes, the leading presentation is spontaneous abortion, preterm labor, or fetal distress [56]. With no major obstetric risk factors, a detailed patient history is mandatory. If there is pallor, watery stools, or abdominal pain, IBD should be ruled out.

#### 21.1.5 Differential Diagnosis

When CD presents with intestinal obstruction, other causes should be excluded (see Chap. 18). Hyperemesis gravidarum and acute pancreatitis can mimic intestinal obstruction.

The first presentation of the ileocecal CD is difficult to distinguish from acute appendicitis, especially because sonographic (US) findings could be similar.

#### 21.1.6 Diagnosis

Scoring systems for assessing the severity of colitis or the failure of medical therapy and laboratory parameters affected by pregnancy are not derived from a population of pregnant patients. They should be used with care [57].

##### 21.1.6.1 Laboratory Findings

Interpretation of blood investigations for IBD during pregnancy can be difficult. Due to hemodilution, hemoglobin and albumin decrease as pregnancy progresses; therefore, they cannot assess the disease activity. Iron deficiency is common because of chronic iron loss. This may be exacerbated during pregnancy; thus, *hypochromic microcytic anemia* is frequently present. Laboratory investigations should include full blood count, urea and electrolytes (potassium, sodium, calcium, and magnesium), liver function tests, erythrocyte sedimentation rate, or C-reactive protein (CRP) ferritin, transferrin saturation, vitamin B<sub>12</sub>, folate, and albumin.

*Leukocytosis* is not diagnostic as this can go up in the second and third trimesters and reach

20,000/mm<sup>3</sup> in early labor in normal pregnancy [58]. *Neutrophil granulocytosis with the left shift* indicates acute (bacterial) infection.

CRP levels are stable (<10 mg/L) during normal pregnancy. CRP can be used to assess disease activity [45]. However, the interpretation is challenging in diagnosing maternal infection postpartum because it rises 10- to 20-fold in normal pregnancy and may increase with neonatal diseases [59]. CRP and serum amyloid A levels in the mother's serum during normal delivery are much higher than in cord blood. There is probably a lack of transplacental transfer of these proteins during labor [59, 60]. Thus, any increase in the newborn CRP and serum amyloid A levels may indicate infection or trauma. On the contrary, the concentrations of TNF- $\alpha$  are higher in the cord than in maternal blood. The concentration of TNF- $\alpha$  in cord blood may originate exclusively from fetal and placental tissues and contribute to neonatal host defense [59, 61].

Patients with small bowel disease or ileal resections are at risk of folate or vitamin B12 malabsorption. Macrocytosis mandates vitamin B12 and folate level measurements.

*Fecal calprotectin*, in combination with the assessment of CD activity, monitors disease activity in pregnant patients with IBD in all trimesters [62, 63]. In addition, increased FC levels predict disease relapse later in gestation [63]. It is a cytosolic protein secreted by macrophages and neutrophils from the inflamed intestinal mucosa. The physiological changes during pregnancy in healthy women do not affect fecal calprotectin concentrations [62]. This is important because other biomarkers, such as CRP, albumin, hemoglobin, and leukocyte counts, change during pregnancy in healthy women and patients with IBD [64]. Fecal calprotectin concentrations are significantly higher in patients with clinically active disease than in remission during the conception period, all three trimesters of pregnancy, and the postpartum period [62]. Normal ranges are not defined, and intraindividual variability of FC levels is well-documented in the general population. It remains to be determined whether serial measurements during pregnancy are beneficial. Deviations from the patient's baseline FC level may indicate disease activity better than using an arbitrary cutoff value [65].

Fecal calprotectin helps with the identification of functional diarrhea. Patients with diarrhea should be tested for *C. difficile* toxin in addition to standard organisms. Four stool samples are required for 90% accuracy [66, 67].

Both osteoporosis and vitamin D deficiency (including compensated deficiency states with normal calcium and high parathyroid hormone) are common with CD. The major risk factors for osteoporosis complicating CD are age, steroid use, and CD activity.

### 21.1.6.2 Imaging Modalities

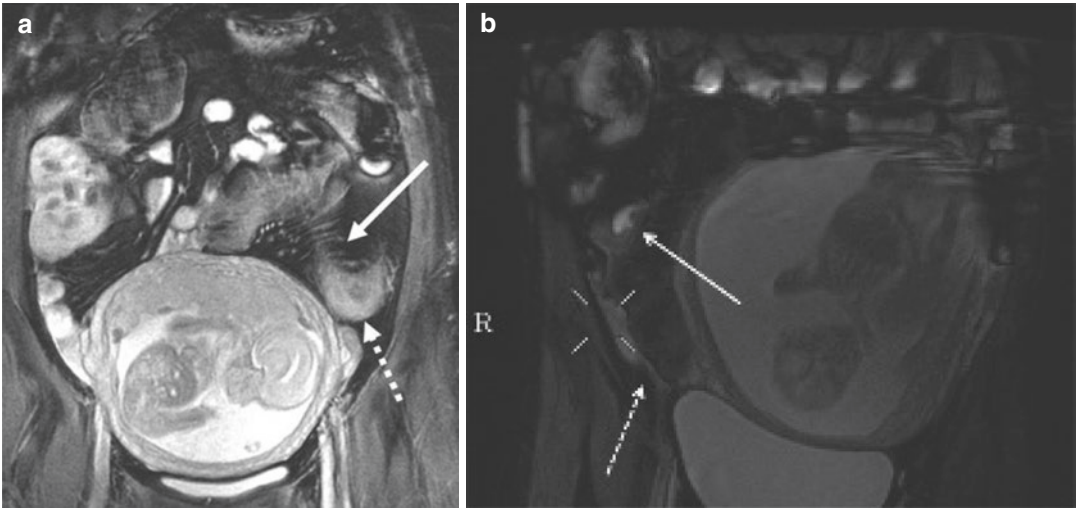
The transabdominal US cannot comprehensively assess the gut. It is the first-line modality for gallstones and kidney stones, which are complications of CD. In expert hands, it has a high sensitivity for detecting disease, particularly the thickening of the terminal ileum wall or the presence of an intra-abdominal abscess. It can exclude acute appendicitis, the most common differential diagnosis.

Both CT enterography and magnetic resonance (MR) enterography (MRE) evaluate disease activity and complications in CD patients in the general population. Abdominal MRI establishes the diagnosis of CD [68]. MR enterography (oral contrast with 5% mannitol 1000 ml, FDA category C) is indicated when abdominal MR is not diagnostic. Different protocols detect urgent surgical complications instead of a dedicated MRE protocol optimized to evaluate signs of luminal and extraluminal disease activity in CD. In particular, safety data about the intravenous contrast material (gadolinium) utilized in MRE are limited, and its use in pregnancy is recommended only when necessary [69]. An additional challenge stems from a significant decrease in image quality due to motion artifacts caused by fetal movements, difficulty in breath-holding, and bowel motion if glucagon is not used. Motion artifacts may be partially overcome with fast-acquired sequences such as FIESTA.

The typical radiographic signs of active CD include (Fig. 21.1) the following:

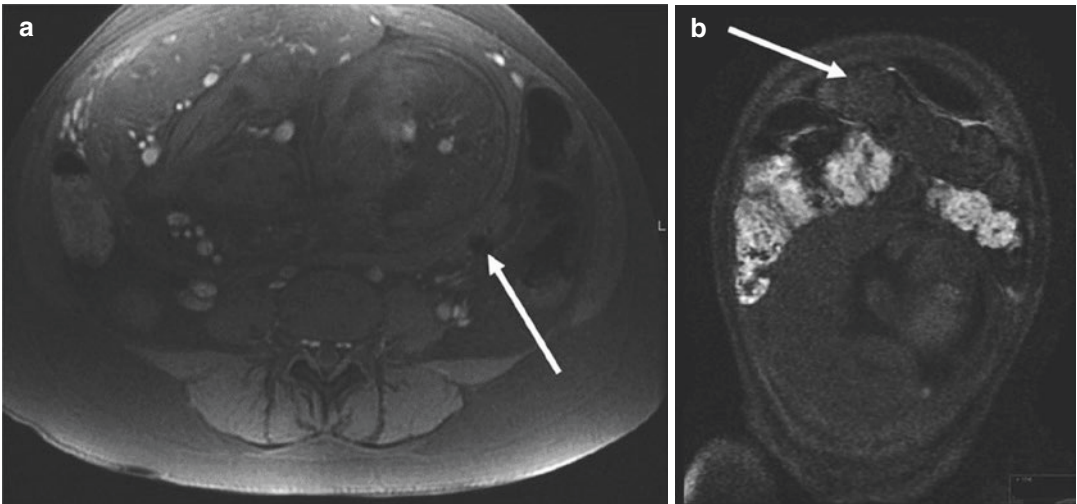
- *Mural Findings*: mural thickening  $\geq 3$  mm, ulcerations, wall edema (high T2 signal on FSE sequence), luminal stenosis, and prestenotic dilation,





**Fig. 21.1** (a) A 19-week pregnant patient with CD, coronal FIESTA: signs of active disease: mesenteric congestion (arrow) and large bowel mural thickening and edema (dotted arrow). (b) A 20-week pregnant patient with CD,

coronal FIESTA: signs of active disease: small bowel mural thickening and an ulcer (arrow), note free fluid (dashed arrow). (Reproduced with permission from [69] under the CC BY 4.0)



**Fig. 21.2** Impact of an enlarged uterus. (a) Axial; pseudo-stenosis (arrow) caused by compressing uterus in 37-week pregnant CD patient. (b) Coronal; a 26-week pregnant patient

with a sigmoid colon displaced cranially (not to be misinterpreted as transverse colon above) (arrow). (Reproduced with permission from [69] under the CC BY 4.0)

- *Mesenteric Findings:* congestion (comb sign), hypertrophy (creeping fat), and lymphadenopathy (lymph node shortest diameter >10 mm),
- *Extraluminal Findings:* phlegmon, abscess, fistula, and free fluid.

This modality can distinguish between CD and UC and accurately estimate disease severity.

This is important, especially in pregnancy, for adjusting drug therapy.

Interpretation of MRE in advanced pregnancy is challenging. The first difficulty relates to anatomical changes caused by the enlarged uterus, such as pseudostenosis and bowel loop displacement. The sigmoid colon may appear stenosed due to the pressure of the uterus (Fig. 21.2a).

Another possible anatomical change is the upward movement of the sigmoid colon cranial to the uterus (Fig. 21.2b), where the sigmoid colon was initially misinterpreted as the transverse colon.

### 21.1.6.3 Endoscopy

Colonoscopy, flexible or rigid sigmoidoscopy in pregnancy, is safe. Endoscopy does not induce labor or significant side effects for the mother or fetus and can be performed safely in medically stable pregnant patients [49, 70]. A colonoscopy with multiple biopsies (at least two biopsies from five sites, including the distal ileum and rectum) is the first-line procedure for diagnosing colitis. It allows the classification of the disease based on the endoscopic extent, the severity of the mucosal disease, and histological features. It also allows the assessment of suspected stenoses in the distal ileum or colon, localizes the source of bleeding, and identifies superimposed cytomegalovirus or *Cl. difficile* infection [70, 71]. Upper gastrointestinal endoscopy should be considered in coexisting dyspepsia.

## 21.1.7 Treatment

### 21.1.7.1 Conservative Treatment

Patients should continue medical therapy in order to induce and maintain remission for as long as possible before the time of conception. Pharmacological therapy for CD during pregnancy is similar to pharmacological therapy for nonpregnant patients. Patients in remission should continue pharmacological therapy throughout their pregnancy, with few exceptions. Approximately 48.6–77% underwent treatment at conception, and 46.9–65% continued medication throughout pregnancy [38, 47]. Most patients received steroids and mesalamine. Only one-quarter was treated with azathioprine or biologic therapy [11, 38].

Two important factors determine the management of a pregnancy in the presence of CD: the disease activity (quiescent vs. active) and when a flare-up occurs—before (fertility), during (early and late pregnancy), or after pregnancy (breast-

feeding). Most medications that treat IBD are not associated with significant adverse effects (Table 21.3).

The greatest risk to the mother and fetus during pregnancy is an active disease, not the medications used to treat IBD. Pregnant IBD patients should not stop maintenance medications during pregnancy and the puerperium due to a high risk of exacerbating disease and complications [72, 73].

### Antibiotics

There is no association between *metronidazole* treatment during all three trimesters of pregnancy and preterm birth, low birth weight, or congenital anomalies [74]. There is an increased incidence of cleft lip or cleft palate in infants of mothers exposed to metronidazole in the first trimester of pregnancy [75]. Metronidazole use in pregnant IBD patients is best limited to short-term use to treat pouchitis. Metronidazole is excreted in breast milk, and breastfeeding during metronidazole use is not recommended [76]. *Quinolone* antibiotics (FDA C) should be avoided due to an increased risk of arthropathy from their high affinity to bone and cartilage. Data on breastfeeding are limited, but quinolone use is probably compatible with breastfeeding [77, 78].

### Aminosalicylates (FDA B)

*Sulfasalazine* (500 mg/day to 6 g/day) consists of sulfapyridine linked to a salicylate radical by a diazo bond. When taken by mouth, only a limited amount is absorbed from the small intestine, and most of the drug reaches the colon intact. It is split at the diazo bond by the colonic bacteria into sulfapyridine and 5-aminosalicylic acid (5-ASA). The sulfapyridine is virtually all absorbed and then metabolizes in the usual way of sulfonamides. Up to 3 g/day is allowed. The 5-ASA is only partly absorbed and rapidly excreted in the urine, so the serum concentration is very low. Maintenance therapy with sulfasalazine through-

**Table 21.3** Medications (alphabetical order) used in the treatment of inflammatory bowel disease

| Drug                          | FDA | Pregnancy                                                                     | Breastfeeding                                                                                           |
|-------------------------------|-----|-------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| Adalimumab                    | B   | Low risk                                                                      | Compatible, clinically insignificant concentration in breast milk                                       |
| Alendronate                   | C   | Fetal skeletal risk                                                           | No human data: probably compatible                                                                      |
| Amoxicillin/clavulanic acid   | B   | Low risk                                                                      | Compatible; enters breast milk                                                                          |
| Azathioprine/6-mercaptopurine | D   | Low risk in monotherapy; delayed infant infections in combination therapy     | Compatible; clinically insignificant concentration enters breast milk; wait 4 h after ingestion if able |
| Balsalazide                   | B   | Low risk                                                                      | No human data: potential diarrhea                                                                       |
| Budesonide                    | B   | Low risk                                                                      | Compatible, clinically insignificant concentration in breast milk                                       |
| Cephalosporins                | B   | Low risk                                                                      |                                                                                                         |
| Certolizumab pegol            | B   | Low risk, crosses the placenta by passive diffusion                           | Compatible, clinically insignificant concentration in breast milk                                       |
| Ciprofloxacin                 | C   | Low risk, potential toxicity to cartilage                                     | Compatible; enters breast milk                                                                          |
| Corticosteroids               | C   | Low risk: cleft palate, adrenal insufficiency, premature rupture of membranes | Compatible                                                                                              |
| Cyclosporine                  | C   | Low risk                                                                      | Limited human data: potential toxicity                                                                  |
| Etanercept                    | B   | Low risk                                                                      | Excreted in milk—probably too large molecule for oral absorption                                        |
| Fish oil supplements          | —   | Safe, beneficial                                                              | Recommended                                                                                             |
| Golimumab                     |     | Low risk                                                                      | Compatible, undetectable                                                                                |
| Infliximab                    | B   | Low risk                                                                      | Compatible, clinically insignificant concentration in breast milk                                       |
| Loperamide                    | C   | Low risk                                                                      | Small amounts excreted in the milk; not recommended                                                     |
| Mesalamine (oral and topical) | B   | Low risk                                                                      | Excreted in milk—if the infant develops diarrhea, discontinue breastfeeding                             |
| Methotrexate                  | X   | Teratogenic                                                                   | Contraindicated                                                                                         |
| Metronidazole                 | B   | Low risk; avoid in the first trimester—the possible risk of orofacial clefts  | Limited human data: potential toxicity                                                                  |
| Natalizumab                   | C   | Low risk                                                                      | Compatible, undetectable                                                                                |
| Olsalazine                    | C   | Low risk                                                                      | Limited human data: potential diarrhea                                                                  |
| Risedronate                   | C   | Experimental animals—skeletal pathology                                       | Excreted in milk—contraindicated                                                                        |
| Rifaximin                     | C   | No human data; animal teratogen                                               | Unknown                                                                                                 |
| Sulfasalazine                 | B   | Low risk. Give folate 2 mg daily                                              | Limited human data: potential diarrhea                                                                  |
| Sulfonamide                   | C   | Not recommended                                                               |                                                                                                         |
| Tacrolimus                    | C   | Low risk                                                                      | Potential toxicity; contraindicated                                                                     |
| Tetracycline                  | C   | Not recommended                                                               | Not recommended                                                                                         |
| Thalidomide                   | X   | Teratogenic; contraindicated                                                  | Limited human data: potential toxicity                                                                  |
| Tofacitinib                   | X   | No human data; animal teratogen                                               |                                                                                                         |
| Ustekinumab                   |     | Limited human data                                                            | Likely compatible; limited human data                                                                   |
| Vedolizumab                   |     | Low risk, limited human data                                                  | Likely compatible; limited human data                                                                   |

Low risk is defined as “the human pregnancy data does not suggest a significant risk to the embryo or fetal harm”

out pregnancy and the puerperium in patients with UC have no noticeable ill effects on the mother or the child [79, 80]. Nevertheless, sulfasalazine and its metabolites reach the fetus in concentrations not greatly different from those in the maternal serum. Although sulfapyridine competes with

bilirubin for the same albumin-binding site, no reports indicate a higher risk of kernicterus in newborns of mothers exposed to sulfasalazine [81, 82]. Sulfasalazine should be stopped if there is suspected neonatal hemolysis. *Mesalamine* proved safe during pregnancy in conventional

(low) doses [83, 84] and even high doses [84, 85]. A few studies reported the risk of neonatal interstitial nephritis with higher doses of mesalazine (>3 g/day) [83, 85]: mesalamine: 1 g orally four times a day; mesalamine, delayed-release tablet: 500 mg orally twice a day; and mesalamine, an enema: one application twice daily (once at bedtime and retained during sleep). Large doses of *olsalazine* (1.6 g orally three times a day) cause birth defects in animals; it is unknown whether *olsalazine* crosses the placenta. The FDA has placed *olsalazine* in risk category C: The drug should be used during pregnancy only if its benefits outweigh the risks. *Topical 5-ASA* has also proved safe and effective in treating women with localized distal colitis/proctitis requiring treatment during pregnancy [86].

The concentrations of sulfasalazine, salazopyrin, and other aminosaliclates and their metabolites in breast milk are 40–50% lower than those of maternal serum and are unlikely to cause harmful side effects [8, 80, 83, 85]. Allergic reactions have been reported in nursing infants as acute watery diarrhea, but this disappears with drug discontinuation [85, 87, 88]. *Olsalazine* may pass into breast milk, and in animal studies, it has been shown to cause slowed growth and other problems during nursing; caution should be exercised when this drug is administered to a nursing woman.

### Electrolytes and Supplements

In a pregnant patient with diarrhea, persistent vomiting, nausea, morning sickness, or ileostomy, it is imperative to restore fluid and electrolytes. Fluid and electrolyte imbalances can occur rapidly under these conditions, causing dehydration.

*Folate supplements*, 2 mg/day, are recommended for all pregnancies to reduce the risk of neural tube defects. These are especially important for those taking sulfasalazine because the sulfapyridine moiety in sulfasalazine competitively inhibits the brush border enzyme folate conjugase [45] and therefore inhibits folate absorption. Other 5-ASA drugs do not contain sulfapyridine and do not carry the risk of folate malabsorption.

*Fish oil supplements* are an adjunct to medical therapy. Supplementation demonstrated prolongation of pregnancy without detrimental effects on the growth of the fetus or course of labor [89]. The FDA does not rate fish oil supplements since they are not classified as drugs.

### Corticosteroids (FDA C)

The moderate-to-severe disease is treated with corticosteroids, which are well-tolerated and relatively safe [90–93]. Although the risk of cleft lip and palate, especially with first-trimester exposure, is often cited [94], the *Committee on Safety of Medicines* in the UK concludes that there is no convincing evidence of such congenital abnormalities being associated with corticosteroids in humans. However, the increased risk appeared in women taking steroids to treat asthma, not IBD. Corticosteroids vary in their ability to cross the placenta; 88% of *prednisolone* is deactivated to a less active metabolite as it crosses the placenta resulting in low fetal blood concentrations. There is no convincing evidence of human teratogenesis [95–97]. If a flare does arise during pregnancy, most patients can be managed successfully with aminosaliclates or corticosteroids, with normal pregnancy and successful delivery [79]. In late pregnancy, newborns whose mothers received high-dose methylprednisolone could develop life-threatening adrenal suppression [98]. These newborns could require *hydrocortisone* supplementation and intensive therapy. Rectal preparations may be used until the third trimester unless there is a specific concern about miscarriage or premature delivery. *Budesonide* should be given, whenever possible, in ileocecal CD [45]. *Budesonide* during pregnancy demonstrated no increase in maternal adverse events when using 6–9 mg/day for 8 months or longer [99].

Corticosteroids are poorly excreted in breast milk (5–25% of the maternal serum concentrations), and the amount received by the infant is minimal. Doses of *prednisolone* up to 40 mg daily are unlikely to cause systemic effects in the infant. Infants of mothers taking higher doses may theoretically have a degree of adrenal suppression, but the benefits of breastfeeding are

likely to outweigh the risks. A 4-h delay following oral exposure has been suggested to minimize fetal exposure [100]. Breastfeeding for mothers on steroids appears to be safe.

### Thiopurines (FDA D)

Immunosuppressive treatment with severe disease is mandatory during pregnancy due to a higher rate of adverse pregnancy outcomes related to disease activity. Although thiopurines are rated FDA class D (positive evidence of human fetal risk, potential benefits may warrant their use), it seems safe and well-tolerated during pregnancy [77]. Thiopurines are transported by passive transplacental transfer. Smaller studies found an increased risk of congenital malformations, perinatal mortality, and preterm birth [101, 102]. In comparison, larger studies did not show statistical differences regarding rates of spontaneous abortion, abortion due to a birth defect, major congenital malformations, neoplasia, or increased infections after the intake of *6-mercaptopurine* (6-MP; standard dose 1 mg/kg) [103–105]. Some conclusions are questioned because of the small number of patients who received 6-MP during the entire pregnancy, with a variable dosage of 25–175 mg/day [106]. AZA (standard dose of 1.5 mg/kg) crosses the placental barrier, but the fetus does not have the enzyme to convert the drug into active metabolites, which explains the lack of adverse effects [107]. The evidence favoring continuing 6-MP and azathioprine (AZA) during the pregnancy is based on the following: (1) Studies have concluded that these drugs are safe; (2) most adverse reactions to 6-MP/AZA occur early, soon after the drug is started. Therefore, the coincidence of any other toxicity to 6-MP in pregnancy could be attributed to active disease; and (3) the most virulent factor with toxic complications during pregnancy is an active CD, and if the patient is in remission just achieved by the drug, it should not be stopped. On the other hand, a study from Lenox Hill Hospital showed a 23% incidence of spontaneous abortions (vs. 13% in IBD controls), a 3% incidence of ectopic pregnancies (compared with none in IBD controls), and finally, an abnormal

amniocentesis in two patients (and none in the IBD controls).

The compromise solutions are as follows: (1) For active CD at conception, if the patient has already been started on the immunosuppressive drug, it should be continued, and the dose even increased if the clinical severity of the disease warrants it; (2) IBD is in remission for months or years, and there is no contraindication to stopping the drug at or before the diagnosis of pregnancy since data have shown that any exacerbation is not likely to occur immediately or for that matter even for months, by which time the pregnancy may be ended or at least the fetus is protected through the first trimester when theoretically it would be most susceptible to any danger. Should an exacerbation occur earlier in the pregnancy, the choice may be made to reintroduce the drug; (3) decisions on whether to continue 6-MP/AZA require rigorous clinical judgment; and (4) a definitive conclusion cannot be drawn due to the dosage differences between the patients and studies. This is an area where rules should not be rigid [8, 102, 103, 108, 109].

If the woman has been in remission for a long time, it seems reasonable to stop the drug until delivery since recurrence is very unlikely. If recurrence develops, the drug can be restarted at that time. If the patients have an active CD or have been in remission only briefly following a severe attack, the continuation of the drug is recommended.

The manufacturers do not advise breastfeeding in patients on AZA and 6-MP. Even though some clinical experiences of mothers who have breastfed on these agents with no apparent adverse effects, breastfeeding is not recommended [110, 111]. An average of 10% of AZA peak plasma concentration levels excretes within the first 4 h after drug intake with a breast milk concentration of <0.008 mg/kg/day [112].



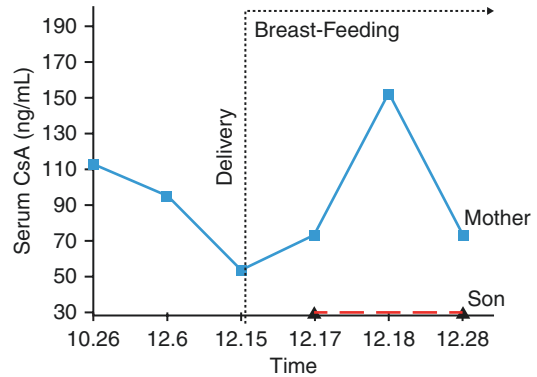
### Cyclosporine (FDA C)

The administration of *cyclosporine A* (iv: 4 mg/kg/day; oral: 8 mg/kg/day) is controversial. In the general population, it induces remission in patients with fulminant UC rapidly and effectively if there is no response to 7 days of IV steroids [113]. Most cases described the delivery of healthy babies [114–118]. Cyclosporine A is highly potent in inducing remission in patients with UC. Despite FDA category C, it seems safe when used at lower doses, approximately 200 ng/ml [117]. In the general population, patients not responding to these agents within 5–7 days should be considered for colectomy, and responders should be closely monitored for infections [119].

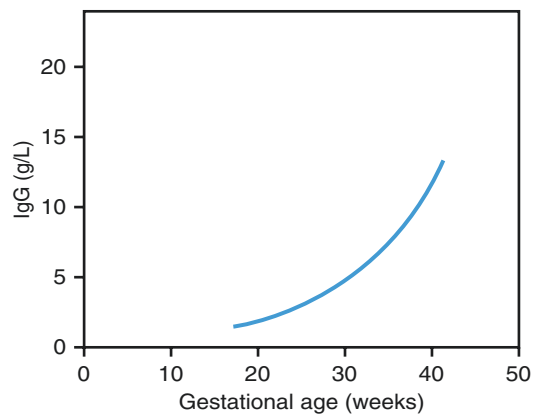
Cyclosporine and infliximab are the leading medical options in pregnant patients with severe steroid-refractory UC. IV cyclosporine has a shorter time to clinical response, but breastfeeding is not recommended because of immune suppression, neutropenia, adverse effects on growth, and carcinogenesis [110, 120]. The dynamics of cyclosporine excretion into breast milk is reported (Fig. 21.3), but neonatal serum levels are mostly low or undetectable without consequences to the baby [121].

### Immunomodulators (FDA B)

In pregnant patients with severe steroid-refractory CD, cyclosporine or infliximab is the main medical option. Infliximab (IFX) has a longer time for response than cyclosporine in severe CD. The chimeric structure of the IFX molecule containing a human IgG<sub>1</sub> constant region limits placental transfer during the first trimester [122]. Preferential placental transport occurs for IgG<sub>1</sub>, followed by IgG<sub>4</sub>, IgG<sub>3</sub>, and finally IgG<sub>2</sub> [123]. Immunoglobulin transport occurs in a logarithmic fashion as the pregnancy progresses, mostly in the third trimester (Fig. 21.4). Therefore, discontinuation of biologics early in the third trimester is posted to decrease the exposure to the fetus because preferential IgG transport is highest during this time [125]. As with other maternal antibodies, IFX has a prolonged half-life in the newborn [125, 126], with persistent thera-



**Fig. 21.3** Maternal and infant serum cyclosporine levels before delivery and 2 weeks into puerperium (units: ng/mL, normal therapeutic range: 100–400 ng/mL). (Reproduced with permission from [118])



**Fig. 21.4** Exponential immunoglobulin G (IgG) transplacental transfer during pregnancy (except for certolizumab). The significant increase is during the third trimester. (Modified and reproduced with permission from [124])

peutic IFX levels in infant cord blood several weeks after cessation of therapy [120, 127]. Maternal transfer of IFX has been reported when doses of 10 mg/kg throughout pregnancy were used. IFX persists in the baby for 7 months [128, 129]. Immaturity of the reticulo-endothelial system leading to slow antibody clearance is probably responsible for this effect. The placental transfer of IFX was not seen when 5 mg/kg doses were used until 30 weeks of gestation [130]. Long-term implications of IFX exposure during early childhood development are unknown.

There is no association between the administration of TNF inhibitors for IBD during pregnancy and adverse pregnancy outcomes or congenital abnormalities. Further, no increased risk of infections has been reported in the first year of life in the offspring of mothers who received biologics [131]. The benefits of achieving and maintaining clinical remission in patients receiving IFX during pregnancy superseded the potential risk of exposing the unborn child to the medication [125].

Non-live vaccines can safely be given to immunocompromised individuals (including neonates exposed to anti-TNF drugs), which mostly lead to an adequate humoral immune response [132]. The 2% receiving IFX at conception discontinued therapy during pregnancy [38]. IFX has not been detected in the human breast milk of nursing mothers [125, 126, 130, 133]. Also, IFX was present in the mothers' sera but not in the infants' sera [130].

The *American Gastroenterology Association* inflammatory bowel disease parenthood working group 2019 recommends continuation of anti-TNFs throughout pregnancy, without interruption in the third trimester, only adjusting last dose timings to achieve the lowest possible trough levels during delivery, with final infliximab infusion given 6–10 weeks before the estimated date of confinement (EDC), final adalimumab injection 2–3 weeks before EDC (1–2 weeks if weekly dosing), and final golimumab injection given 4–6 weeks before EDC [134].

A pregnant woman with treatment-refractory CD who failed with IFX can successfully be treated with *adalimumab*, a recombinant human IgG<sub>1</sub> monoclonal anti-TNF antibody [135]. Infants born to mothers who have received adalimumab up to 56 days before delivery had therapeutic lev-

els of adalimumab in cord blood and serum up to 7 weeks after birth [136]. Adalimumab use during pregnancy is followed by the birth of healthy children [136–138]. Although clinical data are scarce, adalimumab is considered low risk during preconception and at least the first two trimesters of pregnancy [137]. Another case reported the use of *etanercept*, a soluble TNF receptor fusion protein that binds to and inactivates TNF, in an uneventful pregnancy of a patient with refractory rheumatoid arthritis [139]. Etanercept excretes into breast milk, but it is unknown whether the drug can be absorbed orally because it is such a large protein [140]. *Certolizumab pegol*, an IgG<sub>4</sub>-binding pegylated Fab' fragment of an anti-TNF antibody, has less placental transfer than IgG<sub>1</sub> antibodies because it crosses the placenta by passive diffusion as opposed to the active transfer seen in IgG<sub>1</sub> antibodies. *Natalizumab* is pregnancy category C. It is an IgG<sub>4</sub> to  $\alpha$ -integrins and therefore has a different mechanism of action from the other biologics; it also has a different architecture. Pregnancies reported during clinical trials in CD have not led to any signals regarding adverse events, but also the total number of patients exposed is small. Retrospective study [141], small prospective study [142], and pregnancy data collected during the clinical trials program and from postmarketing reports [143] did not identify safety concerns for pregnancy outcomes from direct or indirect exposure to vedolizumab.

### Methotrexate (FDA X)

*Due to the teratogenic and embryotoxic effects of methotrexate, prior to conception, women should discontinue methotrexate for 6 months (GRADE: strong recommendation, low-quality evidence). If patients become pregnant on methotrexate, the drug should be discontinued, and a high dose of folic acid (15 mg daily) should be provided for at least 6 weeks. We suggest that men taking methotrexate may not need to discontinue treatment before conception (GRADE: weak recommendation, low-quality evidence. Agreement: 92.7%) [144].*

### Thalidomide (FDA X)

*Thalidomide* and its analog *lenalidomide* partly counteract the effects of TNF- $\alpha$  and have been used to treat refractory CD in the general population, although currently available systematic evidence does not demonstrate the benefit of these drugs [145, 146]. Thalidomide has extensive teratogenic sequels, including limb defects, central nervous system effects, and respiratory, cardiovascular, gastrointestinal, and genitourinary abnormalities. Thalidomide is contraindicated during pregnancy and breastfeeding. Women of childbearing age taking thalidomide should use two methods of contraception 1 month before starting, during, and 1 month after stopping therapy [145, 146]. If conception should accidentally occur, therapeutic abortion should be discussed, although not mandatory. Although lenalidomide appears less teratogenic in animal studies, exhibiting only teratogenic properties in rabbits at doses with maternal toxicity [77], its structural analogy with thalidomide and the lack of studies demonstrating its safety are absolute contraindications in pregnancy or patients wishing to become pregnant.

### Probiotics

Probiotics approved for managing IBD do not cause any safety concerns for pregnant women [147, 148]. Systemic absorption is rare, and the data do not indicate any increase in adverse pregnancy outcomes [149].

### Enteral/Parenteral Nutrition

Although successful [150–152], total parenteral nutrition is often associated with significant morbidity, including sepsis and catheter thrombosis. For short periods, total parenteral nutrition has been used in pregnancy to treat hyperemesis gravidarum and severe eclampsia and maintain fetoplacental function before delivery. It has rarely been required for longer periods to sustain a pregnancy. Heller, in 1977, recommended avoiding fat emulsion in pregnancy because of the theoretical dangers of maternal ketonemia, premature labor, and placental infarction due to fat emboli.

Enteral treatment with elemental diets seems a safe alternative to total parenteral nutrition in pregnancy [153]. In an uncomplicated CD, remission rates with an elemental diet are 85%, similar to steroids and total parenteral nutrition in the general population [154, 155]. The enteral formulation-based nutrition therapy promotes mucosal healing, reduces the size of abdominal abscesses, has an anti-inflammatory role by altering the gut microbiota, modulates the differentiation of stem cells, and restores the normal morphology of adipocytes [156]. Total peptide formula nutrition therapy, without any other oral intake for 12 weeks, has an 85% remission rate in pregnancy [156]. Peptide-based treatment is indicated for patients with perianal or intra-abdominal abscesses when TNF- $\alpha$  and steroids are contraindicated. Also, there are no adverse effects on the fetus [156]. This finding is important for mothers because many refuse immunomodulatory therapies with potentially adverse effects on the fetus. The maternal effects of elemental diets are presented in Fig. 21.5.

### Antidiarrheal Agents

The routine use of this antidiarrheal is not recommended in nursing mothers: diphenoxylate hydrochloride-atropine sulfate is excreted in breast milk, and atropine may inhibit lactation. Loperamide is transferred into breast milk but is unlikely to affect the child [96].

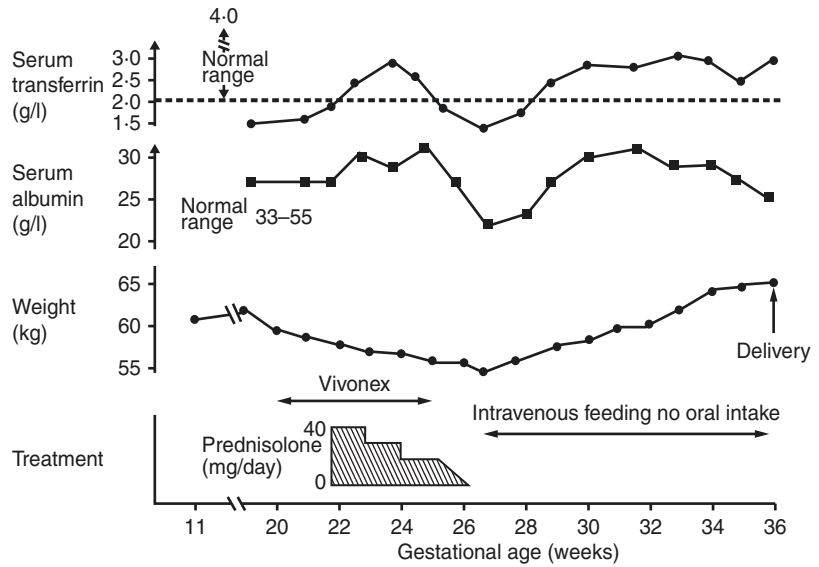
Medical management is presented in Fig. 21.6.

#### 21.1.7.2 Surgical Treatment

Only 2–2.7% of CD pregnant patients require surgery [157, 158]. The approach should be multidisciplinary, and surgery should be performed at a tertiary center with neonatal, pediatric, and obstetric departments.

Indications for surgery in pregnant women with CD are the same as for nonpregnant patients and include intestinal perforation or obstruction, major bleeding, and abscess.

**Fig. 21.5** Progress and treatment during pregnancy complicated with Crohn's disease without and with IV feeding. (Reproduced with permission from [152])



The most common location for surgical intervention is the terminal ileum, either in the form of free or contained small bowel perforation [12] or terminal ileitis with abscesses and fistula or stenosis [11]. Half of the patients were present in the second trimester, with a similar incidence in the first and <10% in the third [11, 12]. Ileocecal resection is the most common (66.7%), followed by small bowel resection (20%), subtotal colectomy (6.7%), and restoration of bowel continuity (6.7%) [11]. A laparoscopic approach is preferred but completed in 10–20% [11–13].

Image-guided percutaneous drainage of an intra-abdominal abscess fails to ameliorate their condition [12] or is a bridge therapy to surgery [11].

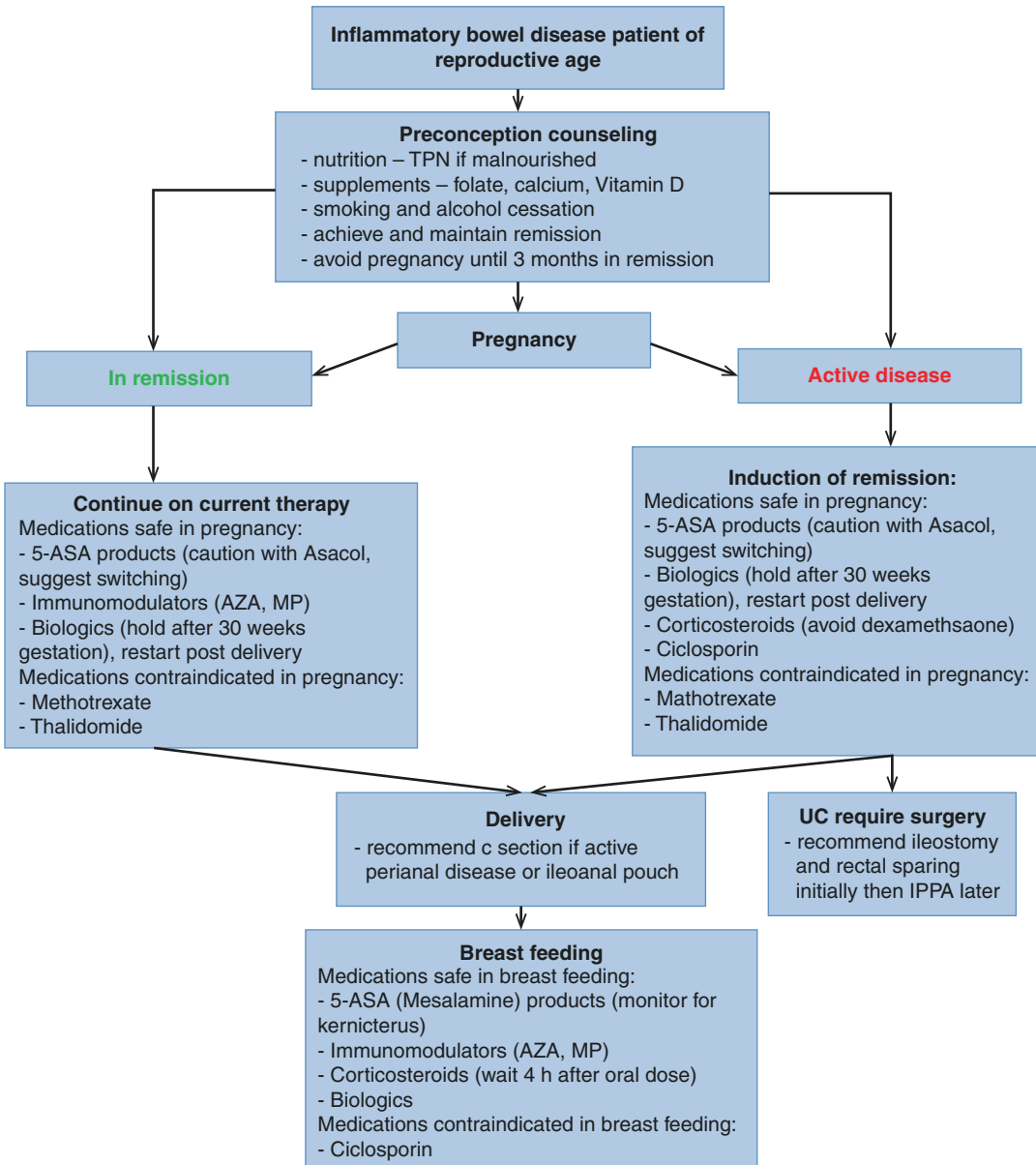
Intra-abdominal surgery performed during the first trimester is associated with an increased risk of miscarriage; the risk is lower for planned procedures in the second trimester. In the third trimester, a laparotomy may be complicated by premature delivery and technical difficulties (see Chap. 4). However, the severity of the CD, not the operation, determines maternal and fetal risks (see Sect. 21.1.7.3). When a woman with a history of CD presents with peritoneal irritation, the severe CD should be considered. In such circumstances, surgery should not be delayed (Fig. 21.7).

## Colorectal Crohn's Disease

- Surgery could be delayed where aggressive medical therapy may allow critical fetal maturation,
- With bowel perforation and diffuse peritonitis, removing the source of sepsis and exteriorizing the bowel ends is indicated [159].

Active intraperitoneal sepsis increases the risk of anastomotic leakage and miscarriage. Intestinal stomas seldom cause difficulty. After delivery, healthy residual bowel can be anastomosed. A stomal therapist should mark the patient before surgery. In pregnant patients, the optimal location for the stoma on the abdominal wall is usually higher than normal because (1) the stoma will drop to a lower position after delivery and (2) to avoid stomal obstruction caused by the growing uterus in the late stages of pregnancy (see Sect. 18.7).

After colectomy, a decision should be made regarding the rectal stump. Stump breakdown and leakage leading to intra-abdominal sepsis are a major concern. The stump can be handsewn in two layers and wrapped with the greater omen-



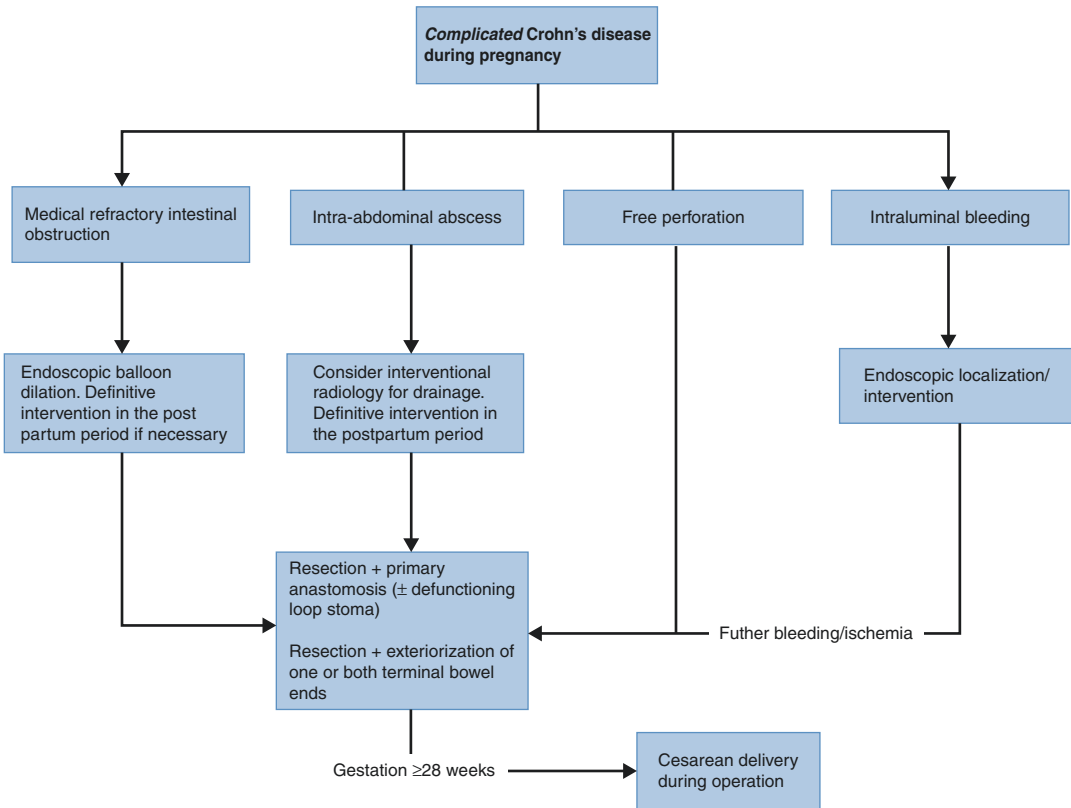
**Fig. 21.6** Decision-making algorithm for the management of pregnancy in IBD patients. *MP* mercaptopurine, *AZA* azathioprine, *5-ASA* aminosalicylates, *IPAA* ileal pouch-anal anastomosis. (Reproduced with permission from [72])

tum or brought out as a mucus fistula. If a mucus fistula is placed, the remnant stump should be kept long. Because of the enlarged uterus, the stump will need to be brought out through an extraperitoneal plane deep into the broad ligament and dilated ovarian vessels. The rectum is irrigated during the surgery to remove the excess

bloody mucoid material and a rectal tube to keep it decompressed in the postoperative period [160].

It is undefined when to continue medical therapy after IBD surgery during pregnancy and whether this interval without medical therapy influences disease activity during further pregnancy.





**Fig. 21.7** Treatment algorithm for patients with complicated Crohn's disease during pregnancy and the puerperium. (Modified and reproduced with permission from [12])

### Small Bowel Crohn's Disease

The indications for small bowel surgery in pregnant women with CD are not different from the general population and include intestinal obstruction or perforation, bleeding, or abscess. Budesonide should be given, whenever possible, in ileocecal CD [45].

A temporary ileostomy is preferred to reduce the risk of postoperative complications of primary anastomosis [12], although 66% of the anastomotic rate has been published [11].

### Presentation Mimicking Acute Appendicitis

There are several issues here. The first issue is an abdominal wall incision. If acute appendicitis is suspected, laparoscopic exploration is recommended. If an indication for bowel resection exists (abscess adjacent to active ileocecal disease, bowel perforation, bowel obstruction), ileocolic resection can be completed by laparoscopy or conversion to median laparotomy. Another issue is bowel resection when the active ileocecal CD is present without perforation, obstruction, or adjacent abscess [161]. During exploration for active disease, resection is preferable to prevent exacerbation during further pregnancy.

### 21.1.7.3 Obstetric Management

#### Mode of Delivery

In 1972, the authors stated that in the case of an unplanned pregnancy occurring in a patient with active CD whose family is already complete, there are strong indications for suction termination in the first trimester [162].

Pregnancy termination should never be considered a therapeutic option for CD flare-ups, as there is no evidence to suggest that induced abortion improves disease activity.

*The Royal College of Obstetricians and Gynaecologists and the American College of Obstetricians and Gynecologists* do not have particular guidelines on pregnancy and CD. There is an increased rate of CS in women with IBD [163] for both CD (aOR 1.72) and UC (aOR 1.29) compared to non-IBD controls [164]. The CS rate is higher in CD patients while at baseline in UC patients [165]. Over half of all CS in patients with IBD are emergent and performed for high-risk obstetric or neonatal outcomes such as arrest of descent or cervical dilation and nonreassuring fetal heart rate tracings [166]. The risk of incontinence and anal sphincter tears is less in CS than in vaginal delivery [167–170], although vaginal delivery reduces the rate of surgical procedures and adhesion formation [171].

Disease progression within 2 years after childbirth was significantly more frequent with the active luminal disease before pregnancy, independent of the mode of delivery [26]. This suggests that CS does not prevent the worsening of CD over a median follow-up of over 4 years [172]. Surgery at all stages of pregnancy resulted in a 50% rate of CS commonly performed simultaneously with surgery for the CD with a viable fetus [12].

The delivery mode does not influence the natural history of IBD. Vaginal delivery is not associated with an increased risk of subsequent perianal disease in women with CD. Vaginal delivery should be preferred in patients with ileostomy and no active perianal disease.

#### Elective Cesarean Section

In general, the indications for elective CS are *ECCO guidelines*, *Toronto Consensus Statements*, and the *British Society of Gastroenterology* [144, 173, 174]:

- Obstetric,
- Active perianal disease (abscess or fistula),
- Rectal involvement or rectovaginal fistula,
- IPAA or ileorectal anastomosis.

Preexistent perianal disease is present in 25% of patients [26]. Patients with inactive perianal disease or no history of the perianal disease are not at increased risk for the perianal disease after vaginal delivery. Patients with active disease had worsening symptoms in two-thirds of cases [175]. The progression of perianal disease was observed significantly less frequently after vaginal delivery than after CS, with the same trend in patients with and without perianal disease before pregnancy [26, 28, 176]. These results should be taken with caution because indications for CS could be confounding. The strongest predictors of CS are a history of the perianal disease (aOR 13.6) and prior CS (aOR 22.2). Among women who underwent CS because of perianal disease, only 42% had active perianal symptoms during pregnancy [177].

Another issue is whether episiotomy added to vaginal delivery increases the rate of perianal disease. Episiotomy, perianal tears, and instrumental delivery do not influence the incidence of perianal CD [175]. Women with IBD (both assisted reproductive techniques (ART) and spontaneous pregnancies) had a higher rate of elective CS in comparison to women undergoing ART and those with spontaneous pregnancies [178].

#### Emergent Cesarean Section

In patients presenting with peritonitis or non-stomal intestinal obstruction, the treatment depends on the trimester of pregnancy. Only the cause of an acute abdomen is treated surgically during the first two trimesters. After surgery without CS, fetal monitoring starts in the recovery room for spontaneous labor. After 28 weeks of pregnancy, emergent CS during operation for acute CD is recommended due to a higher incidence of postoperative complications leading to spontaneous induction of labor [160, 179]. Up to 2017, for all emergently operated CD patients, the rate of CS was 50% [12].

### 21.1.8 Prognosis

#### 21.1.8.1 Maternal Outcome

##### Morbidity and Mortality

Increased maternal morbidity is due to the consequences of acute abdominal conditions requiring emergency surgery, the underlying chronic inflammatory condition, and its comorbid conditions. Perioperative complications mainly depend on the severity of CD. There are no comparisons between open and laparoscopic procedures. There is a threefold increase in the incidence of gestational diabetes in patients with IBD compared to healthy controls, regardless of gestational corticosteroid use [180]. Possible mechanisms for an increased risk may include vitamin D deficiency [181] and an increase in the transcription factor 7-like 2 gene variant, implicated in both CD and gestational diabetes [182, 183]. There is a significantly higher rate of gesta-

tional diabetes among UC patients using ART than CD patients (29.4% vs. 6.1%) [178].

Higher maternal thromboembolic complications and malnutrition/poor weight gain in pregnant IBD patients are confirmed [164, 184].

The maternal outcome showed no difference regarding preterm birth and pregnancy complications between CD patients who conceived spontaneously and CD patients using ART [178].

The patients with ileostomies are capable of normal pregnancies [93, 185, 186] but have lower hemoglobin levels during pregnancy [187], apparently without ill effect. Stomal problems of displacement and prolapse are not uncommon but remit postpartum. Vomiting during pregnancy can cause stomal prolapse requiring revision after delivery.

In 1972, there was a concern about abscess and fistula formation because, in the puerperium, the rapid involution of the uterus may tear apart adhesions that wall-off abscess cavities, leading to spreading peritonitis [162].

Before 1946, maternal mortality from CD was 40% [10]. During the 1960s, the mortality rate doubled compared to the general population [91, 188]. Later studies found similar rates of maternal mortality. It might, therefore, be assumed that conception took place more readily in these patients whose disorder was less florid. Until 1962, maternal mortality from the first episode of surgically treated terminal ileitis was 14% [50]. Since 1983 maternal mortality in operated CD patients has been 0% [12], although a French national study (1992–2015) reported 6.7% [11].

##### Fertility and Sexual Health

Older studies [91, 186], including Crohn and Korelitz in 1956 [15], claimed that fertility is subnormal, but the interrelation is complex. Three principal CD-related factors for impaired fertility are (1) active disease, (2) pelvic surgery, and (3) loss of self-esteem, libido, and fear of pregnancy outcomes. Active disease is responsible via multiple mechanisms, such as pelvic inflammation, poor nutrition, decreased libido, dyspareunia, and depression [189]. The symptoms of CD, including diarrhea, problems with continence, and weight loss, affect body image,

particularly in adolescents and young adults. The side effects of treatment, such as weight gain due to steroids, may also cause feelings of unattractiveness and loss of self-esteem. Children with CD may experience delays in growth and puberty, which also seriously affects confidence and body image. Young people with IBD may experience difficulty forming intimate relationships and worry that they may not be able to have a normal sex life. The result is decreased libido. In older studies, vitamin B<sub>12</sub> deficiency occurred in 60% of patients [15], commonly in patients with intestinal resection. Some patients became pregnant within six months of starting vitamin B<sub>12</sub> therapy. Systemic effects of the disease, for example, fatigue and anemia, as well as medication effects, such as corticosteroids, can impact libido and sexual activity. This explains that adequate nutrition with correcting deficiencies is therapeutic in terms of fertility.

Fear of inheritance of IBD in the offspring and fear of fetal exposure to IBD therapies can lead to voluntary childlessness. Stoma surgery is a major life event, particularly for teenagers [190]. The development of IBD may put great strain on a previously good relationship. Women in a relationship experience more difficulties in their sexual life than nonaffected women of a similar age [191, 192].

Postoperative dyspareunia can similarly affect sexual activity and the chance of conceiving [91]. Dyspareunia, the involvement of the fallopian tubes in the disease process, general ill health, and medical advice against pregnancy have all been implicated [8, 193]. Dyspareunia and vaginal candidiasis are more common than in healthy women, accounting for some difficulties [194]. Many women experience changes in their menstrual cycle in the year preceding IBD diagnosis. Changes in cycle length were most common, followed by changes in flow duration and menstrual pain [195–198]. Although the potential causes of menstrual irregularity are vast, it has been suggested that the menstrual cycle is an additional vital sign in assessing well-being and excluding pathological conditions [199]. Thus, eliciting if a woman with suspected IBD has experienced changes in her menstrual cycle may provide the

clinician insight into the nature and severity of the underlying disease. Most women with baseline dysmenorrhea who experienced a change reported their menstrual pain to be more intense and longer in the year before IBD diagnosis. This finding may be because of pathophysiologic mechanisms common to IBD and primary dysmenorrhea. Some authors have speculated that when released from sloughing endometrium during menstruation, prostaglandins induce uterine contractions and menstrual pain [200] and may also play a role in the abdominal pain and diarrhea experienced by IBD patients due to increased contractility of gastrointestinal smooth muscle [201]. Alternatively, this finding may be due to the misperception of IBD symptoms as worsening menstrual pain. Given the overlap in symptoms between active IBD and dysmenorrhea (e.g., nausea and vomiting, loss of appetite, diarrhea, general aching, irritability, sleep disturbances, and depression), symptom confusion may certainly occur.

If endometrial thickness, an important determinant of fertility, and in vitro fertilization (IVF) success and hypothalamic/pituitary hormone release are truly unaltered in IBD, this will correlate with the normal fertility rates for women with IBD who have not undergone surgery [202, 203]. It would also suggest that women with IBD undergoing IVF are not at decreased odds for endometrial implantation or IVF success. Cycle regularity changes significantly over time, wherein more regular cycles were found for each year of greater disease duration. This is an important finding for young women desiring natural pregnancy because it can reassure them that their cycles should become more predictable over time. Although IBD treatment and disease control may play a role, cycle regularity improved regardless of disease activity and after controlling for changes in BMI. Steroid use is associated with more irregular cycles, even after adjusting propensity scores [195].

Fertility appears to revert to normal after remission induction in women with CD. Women who have their first pregnancy after the onset of IBD have fewer pregnancies than population controls. In contrast, women who became preg-

nant before the onset of IBD have a similar reproductive history [202]. Also, women with CD have a delayed age of first pregnancy after being diagnosed [204] and have fewer children than might be expected after diagnosis, with a higher rate of failure to conceive [193]. These are probably some reasons for the lower incidence of IBD in pregnancy.

Surgery for CD may decrease fertility compared with medical therapy alone. The development of postoperative pelvic adhesions contributes to a higher infertility rate [203]. On the contrary, patients undergoing resections could have higher pregnancy rates due to eliminating the active disease and subsequent nutritional deficiencies [186]. If the disease is not active sexual desire rises. CD patients had a higher rate of birth control, were having sexual relations, and were advised by their physicians not to become pregnant. Patients with CD had a notable reduction in the number of children.

With adequately treated and nourished pregnant CD patients, there are similar infertility rates compared with the general population (5–14%) [17, 202, 203]. Subfertility is common with active CD [47, 193].

### 21.1.8.2 Fetal Outcome

#### Inheritance of CD

Patients are naturally concerned about passing their disease on to their offspring. Unfortunately, family history is the strongest predictor of developing IBD. If one parent is affected, the risks of the offspring developing IBD are 2–13 times higher than in the general population [205–207]. One study estimated that the risks of IBD in first-degree relatives of probands with UC and CD were 1.6% and 5.2–7.5%, respectively, and even higher values in the Jewish population [30, 207, 208]. If both parents have IBD, the risk of their offspring developing IBD during their lifetime was estimated to be 35% [207, 209].

Breastfeeding may protect against the development of IBD in infants, with a pooled odds ratio of 0.45 (0.26–0.79) for CD [210]. However, these were not mothers who had IBD themselves.

#### Perinatal Outcome

Crohn et al., in 1956, considered that the percentage of stillbirths, miscarriages, or spontaneous abortions is not increased [15]. The abortion rate in patients with CD in the 1960s was 13–15% [15].

Pregnancy outcomes depend on the disease activity during conception or pregnancy, not the operation.

Patients whose CD is in remission at conception have pregnancy outcomes similar to those in the general population [27, 211]. Adherence to screening guidelines for gestational diabetes during pregnancy—testing at 24–28 weeks of gestational age [212] and optimizing vitamin D levels may improve fetal outcomes in patients with IBD. Fortunately, there is no increased risk of placental-related disorders in patients with IBD [166].

Active disease at conception is associated with a higher rate of fetal loss, preterm birth (twofold), LBW (threefold), and small for gestational age infants [24, 41, 44, 45, 93, 160, 162, 207–210]. Women with CD have 1.9 times the risk of abdominal wall defects [213]. The association between CD and abdominal wall defects was more prominent in women whose first CD diagnosis was after delivery, suggesting that these women may have had mild, undetected inflammation during pregnancy or that other pathways are involved. The association was weaker after 2000, suggesting that it is unlikely that biologics increased the risk of wall defects and that folic acid food fortification could have been beneficial [213]. Preterm delivery is further associated with disease flares during pregnancy [41, 214]. The preterm delivery rate among surgi-



cally treated patients is 79% [12]. Increased circulating prostaglandin levels during a flare could initiate preterm labor with the induction of smooth muscle contraction [215, 216]. Another theory is that the role of increased gut permeability during increased inflammation could alter nutritional and immunological factors affecting labor [215]. Other predictors of an adverse outcome include ileal CD [184] and previous bowel resection [184, 211]. In the general CD population, smoking is a known risk factor for LBW infants, preterm delivery, and disease activity [9, 217]. After 2000, there was no increase in small-pox incidence for gestational age [165].

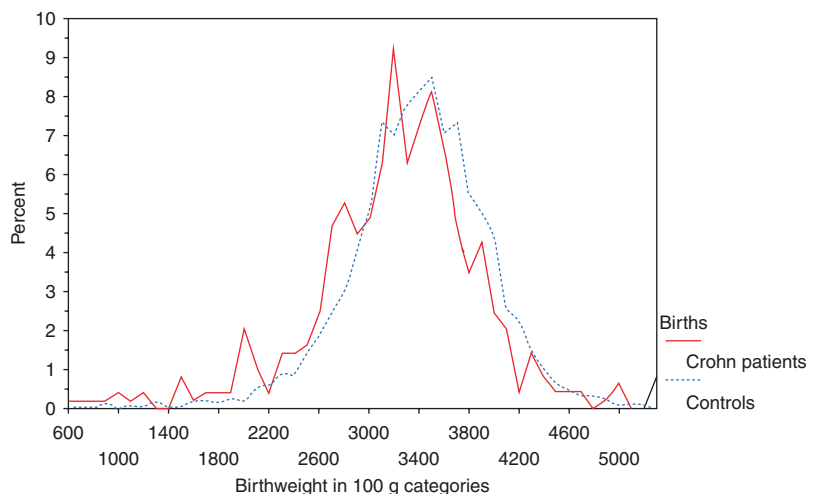
Subclinical infection is another issue. Although the women are free of symptoms at the beginning of the pregnancy, subclinical inflammation found on colonoscopy with biopsy could explain the higher rate of small for gestational age births [184]. These women felt too well to present for investigation; therefore, these data are unavailable.

Infection and inflammation, in general, have been correlated with an increased risk of pregnancy complications such as preterm birth and premature rupture of membranes (see Chap. 4). Possible candidate genes in the cause of preterm birth include TNF- $\alpha$ , TNF receptor 1, and TNF receptor 2 alleles [218], suggesting another possible link with IBD.

A meta-analysis including more than 700 patients with CD reported a normal pregnancy in 83% (71–93% in individual studies). Fetal malformations were observed in 1% of all pregnancies. The frequency of spontaneous abortions and stillbirths was similar to that observed in the general population [219]. Studies with all CD subgroups during pregnancy did not find significantly different perinatal outcomes (105–142 g less than children born to mothers without CD and a higher risk of LBW and preterm birth) compared to the general population even before the era of biologics (Fig. 21.8).

Predictors of poor outcome (preterm birth, LBW, intrauterine growth retardation, small for gestational age infants, congenital anomalies, APGAR scores, stillbirth, and labor complications) are having active CD, previous surgery for CD, and nonwhite ethnicity [211, 221]. The typical resection area is the terminal ileum, and loss of the terminal ileum's capacity for nutrient and vitamin absorption could predispose to a smaller birth weight. Secondly, the fact that resection had previously occurred may serve as a marker of greater disease severity. The rate of previous surgery for CD is similar between pregnant women and nonpregnant women with CD [24]. There is a correlation between the length of bowel resection or active disease at conception and an increased risk of spontaneous abortion compared to a refer-

**Fig. 21.8** Distribution of birth weight in babies born of mothers with Crohn's disease and babies born of a control group. (Reproduced with permission from [220])



ence population and women with UC [40]. Patients operated on during pregnancy after 1983 had a premature delivery rate of 40% [12].

Primiparous CD patients have a higher birth weight decrease than multiparous CD patients [44]. Abnormal birth weight, stillbirth, spontaneous abortion, and congenital abnormalities (contrary to the patients with UC) are no more common (in inactive disease during pregnancy) than in the population without IBD [17]. A population-based study from Denmark also did not find an increased risk of adverse events associated with disease activity [222]. They reported that women with active disease had mean adjusted risks of LBW, LBW at term, preterm birth, and congenital anomalies of 0.2, 0.4, 2.4, and 0.8, respectively. However, the crude risk of preterm birth was increased, with an odds ratio of 3.4 in those with moderate to high disease activity.

The difference in the distribution of the CD lesions may be a significant factor for different perinatal outcomes. Surgical intervention for large bowel CD has a worse perinatal outcome than ileal CD [159, 223]. With the resection of terminal ileitis, fetal mortality is 0% [159]. One explanation for the worse perinatal outcome with colonic CD is the higher rate of postoperative complications [159, 223].

Until 1962, all women with the first episode of surgically treated terminal ileitis delivered prematurely, and perinatal mortality was 43% [50]. After 1983, perinatal mortality in operated CD patients during pregnancy was 5%, while premature birth was 79% [12].

### Breastfeeding and Vaccination

Although the *American Academy of Pediatrics* recommends breastfeeding for at least 6 months after birth [224], many women who require drug therapy initiate breastfeeding less frequently and discontinue breastfeeding earlier than women who are not receiving medication [225] or do not breastfeed at all [43]. First, breastfeeding protects against immune-mediated diseases such as bronchial asthma, atopic dermatitis, allergic rhinitis, and type 1 diabetes mellitus. This effect is attributed to the immunomodulatory properties

of human milk. Heredity has its role in developing IBD; however, environmental factors (such as smoking status) are also important [226, 227]. Some data suggest that breastfed infants may be at decreased risk [208], and others claim a statistically significant protective role against UC and an even greater role against CD [210]. Therefore, breastfeeding minimally for 6 months and up to 2 years is recommended. Currently, it is unknown whether the absence of breastfeeding and the presence of bottle feeding are risk factors for IBD [210].

Avoid live virus (including BCG and rotavirus) vaccines in the first 6 months with *in utero* biologic agents exposure (except certolizumab) or until biologics are no longer detectable in the child's blood. Live vaccines at one year (MMR, varicella) can be given even in breastfeeding infants of mothers on biologics [134, 144].

## 21.2 Ulcerative Colitis

### 21.2.1 Incidence

UC was first described by the British physician Sir Samuels Wilks in 1859 [228]. A. M. Gossage and FW Price noted an association between UC and pregnancy (four patients developed UC during or just after pregnancy) at a symposium at the *Royal Society of Medicine* in 1909 [229]. Further descriptions were by Yeomans in 1921, Barnes and Hayes in 1931, and Bergen et al. in 1939.

UC preferentially affects women between the ages of 20 and 39 and does not impair fertility. Estimation from 1956 was that up to 50% of females who develop UC before 45 would subsequently become pregnant [230]. The first description of two cases of toxic megacolon due to UC was by Thomas Holzbach in 1969 [231]. Up to 7% of patients will present the first UC episode during pregnancy or the puerperal period [97].

Although UC and pregnancy frequently coexist, it is rare for fulminating disease to ensue and

require an operation to save the mother's life before or after delivery. Up to 2017, 56 cases of UC were managed by surgical intervention during pregnancy with a median age at presentation of 25 (21–35) [12]. Ten presented in the first trimester, 19 in the second, and 13 in the third. Four patients presented in the immediate postpartum period. Fourteen patients had been newly diagnosed with UC during pregnancy, and others had preexisting UC [12].

### 21.2.2 Effect of Pregnancy

Disease in the general population is classified into mild, moderate, and severe for management and prognostic purposes according to *Truelove criteria* based on bowel movements per day, fever, heart rate, anemia, and sedimentation rate [232]. The classification from 1951 by Abramson et al. is in four categories [18]:

- Category I—inactive at conception,
- Category II—active at conception,
- Category III—arising during gestation,
- Category IV—arising during the puerperium.

Up to the early 1950s, up to 90% of patients relapse during pregnancy [18]. After the 1980s, there was a 30–50% chance for female patients with UC to have an exacerbation during pregnancy or early postpartum [233]. Willoughby and Truelove found that patients with UC who had the inactive disease at conception tended to remain so during the pregnancy. In contrast, those with active disease had continued and even worse disease activity [97]. Around 50% of active cases had improvement; in all cases, it was by the end of the eighth week of pregnancy [93]. Nielsen et al. reported an exacerbation rate of 34% per year during pregnancy and 32% per year when not pregnant in women with UC [92]. Relapse occurs mostly in the first trimester, but the risk to

the mother is negligible, provided that the UC is treated vigorously [30, 92, 203, 234].

Currently, women with IBD are as likely to flare during pregnancy as they are when not pregnant; around 30% with inactive UC at the time of conception would develop an exacerbation during pregnancy or the puerperium [97, 235, 236], a figure close to the expected recurrence—the rate in a comparable group of nonpregnant women [92, 234, 237]. During those decades, two-thirds of patients remained symptomatic or deteriorated with active UC at conception [97].

The effects of multiple pregnancies on UC do not show a definite pattern, and there is an agreement that there are no consistent effects in successive pregnancies [93].

Relapses of UC usually occur in the first trimester or the puerperium [20, 97, 235, 236, 238, 239]. The high circulating levels of serum 17-hydroxycorticosteroids during the second and third trimesters induce remission [15, 237]; levels fall sharply following delivery. Although cortisol comprises 90% of total plasma 17-hydroxycorticosteroids in the third trimester of pregnancy, the increase is due to elevated levels of the glucocorticoid-binding protein transcortin. Biologically active cortisol remains unchanged [236], and there is no increased steroid action in pregnancy. A small prospective study reported a decrease in relapse rate in UC patients 4 years after pregnancy compared with the 3 years before pregnancy [46]. The relapse rates decreased following pregnancy compared to prepregnancy (0.34 vs. 0.18 flares/year) [47]. Severe colitis during pregnancy is rare [240]. Interestingly, a study from Greece found a higher incidence of smokers among pregnant IBD patients in the quiescent phase (43%) than in normal pregnant women (14%). However, the difference was insignificant due to the small number of patients [24].

The only prospective study reported disease activity in pregnant women with UC compared to nonpregnant women with UC [38]. Approximately 84% underwent therapy at conception, and 86% received treatment during pregnancy. Only 65%

in remission at conception remained in remission, compared to 82% of the nonpregnant control ( $p < 0.0001$ ). HR 2.74 was found for a disease flare during pregnancy. Women were more likely to experience a flare in the first and second trimesters and the first 3 months following delivery than during the third trimester. Interestingly, if a woman had the active disease during the first trimester, her risk of continued activity was no higher than matched controls.

In conclusion, UC has a higher risk of disease activity than CD [52]. It is unclear why UC might be so unstable during pregnancy. However, one theory is that the shift in the immune environment from one rich in TH<sub>1</sub> cells to one dominated by TH<sub>2</sub> cells promotes disease activity. This shift is caused by a maternal response to the fetus, as a bias toward a TH<sub>2</sub> state is protective of pregnancy [241].

*If conception occurs at a time of quiescent disease, the risk of relapse is the same as in nonpregnant women. Conception occurring at a time of active disease increases the risk of persistent activity during pregnancy. Pregnancy may influence the course of ulcerative colitis. (ECCO, 2017 [242])*

21.2.3 Classification

All new patients should have their disease phenotype classified under the *revised Montreal Classification* (Table 21.4). Classification attempts to characterize the clinical patterns of UC [53, 54] more accurately. Also, it serves for a better understanding of the disease dynamics during pregnancy, treatment options comparison, and prognosis.

**Table 21.4** Definition of ulcerative colitis phenotype according to the Montreal classification

| The extent of inflammation at colonoscopy    |    |
|----------------------------------------------|----|
| Proctitis                                    | E1 |
| Left-sided e extending up to splenic flexure | E2 |
| More extensive disease                       | E3 |

(Reproduced with permission from [53] under the CC BY 4.0)

21.2.4 Pathophysiology

21.2.4.1 Free Intestinal Perforation

As for the CD, there are several mechanisms. First, these include perforations due to the primary disease itself; second, perforations after earlier surgical procedures; and third, during labor. This third mechanism is fundamental because it includes several interrelated mechanisms. If the CS is indicated in a patient after previous surgery for UC, intestinal adhesions can obstruct the location for uterotomy. Therefore, adhesiolysis can be mandatory and can result in the opening of the bowel wall. Another possible mechanism that damages the bowel serosa results in delayed intestinal perforation. The third pathophysiology can result after the avulsion of the ileal wall by the rapid retraction of the uterus in the postpartum period both after CS (especially after the previous operation for UC) [243] and vaginal delivery.

21.2.4.2 Toxic Megacolon

This condition is characterized by severe transmural inflammation with infiltration of the colonic wall by neutrophils, lymphocytes, histiocytes, and plasma cells. Toxic megacolon results from a severe inflammation extending through the smooth muscle layer, possibly causing paralysis of colonic smooth muscle resulting in marked dilation. There is a correlation between the depth of invasion and the degree of colonic dilation. Neutrophils invade the muscle layer and release proteolytic enzymes, cytokines, and leukotrienes. Nitric oxide, an inhibitor of smooth muscle tone, is released from neutrophils and leads to colonic dilation. Inflammation and upregulated nitric oxide synthetase increase local nitric oxide, inhibiting colonic smooth muscle and causing dilation [244, 245]. Myenteric plexus involvement is inconsistent and probably does not contribute to bowel distension.

Additional factors could also play a role in colonic dilation. Some are specifically associated with pregnancy: (1) tocolysis with ritodrine [231, 246], (2) mechanical obstruction due to an over-distended uterus and bed rest [246], and (3)

progesterone-induced smooth muscle relaxation. General factors not specific to pregnancy that can precipitate toxic megacolon are (1) anticholinergics, (2) narcotics, (3) hypokalemia, and (4) barium enema.

Anemia is common during pregnancy associated with IBD, and regular surveillance to exclude this may be advisable [187].

### 21.2.5 Clinical Presentation

Of all 56 surgically treated patients during pregnancy, 14 had been newly diagnosed with UC, and the median duration of symptoms for those with preexisting UC was 8 (0–13) years [12].

#### 21.2.5.1 Elective Presentation

If there is a history of prepregnancy UC, then symptoms suggestive of UC can confirm the diagnosis and speed up the diagnostic workup. The diagnosis is challenging if UC presents for the first time during pregnancy. Symptoms and signs suggestive of UC are the same as in the nonpregnant population: tenesmus and increased stool frequency with the passage of blood and mucus.

Symptoms and signs of extraintestinal manifestations (found in both UC and CD) should be sought. Musculoskeletal—arthritis, spondylitis, and sacroiliitis; dermatologic—erythema nodosum, pyoderma gangrenosum, psoriasis, oral aphthous stomatitis, and Sweet syndrome; hepatopancreatobiliary—primary sclerosing cholangitis, cholelithiasis, portal vein thrombosis, drug-induced hepatotoxicity, and drug-induced pancreatitis; ocular—episcleritis, scleritis, uveitis, and conjunctivitis; renal—nephrolithiasis, obstructive uropathy, fistulization of the urinary tract, and secondary amyloidosis; and pulmonary—chronic bronchitis, subglottic stenosis, bronchiectasis, and bronchiolitis. There are no data on an increased or decreased incidence of extraintestinal manifestations of UC or CD during pregnancy.

Osteoporosis and vitamin D deficiency (including compensated deficiency states with normal calcium and high parathyroid hormone)

are common with UC. The major risk factors for osteoporosis complicating UC are age, steroid use, and UC activity.

#### 21.2.5.2 Emergent Presentation

As in the nonpregnant UC population, several presentations require emergent management: profuse intractable intraluminal mucosal bleeding leading to hemorrhagic shock, intestinal obstruction, bowel perforation with symptoms and signs of peritonitis, and toxic megacolon with progressive dilation of the colon with increasing abdominal pain with abdominal distension with antecedent bloody diarrhea [247]. Nausea and vomiting can be present in intestinal obstruction (more exaggerated with feculent vomitus) and toxic megacolon.

#### Toxic Megacolon

Sometimes, it is difficult to differentiate between large bowel obstruction and toxic megacolon. The previous clinical presentation is a clue to the diagnosis. Before clinical deterioration, the patient has typical UC symptoms (diarrhea, bloody or non-bloody, abdominal pain, fever) and progression of abdominal pain with colonic distension [247]. The physical examination can reveal localized guarding with rebound tenderness and diminished bowel sounds [231, 247, 248]. Similar signs can be found in the early phase of intestinal perforation, while in advanced bowel obstruction, bowel sounds are absent.

### 21.2.6 Differential Diagnosis

#### 21.2.6.1 *C. Difficile*-Associated Toxic Colitis

Historically, both peripartum *C. difficile*-associated disease and the disease during pregnancy have been considered an unusual occurrence and, when present, has generally been mild disease. However, in 2005, a concern was raised [249] about a possible increase in the frequency and severity of *C. difficile*-associated disease in pregnant women, including severe complications such as those resulting in inten-



sive care unit admission, toxic megacolon, colectomy, death, and fetal loss. The pathophysiology of the infection in pregnancy remains poorly understood [250]. Although antibody production generally increases during pregnancy, this production may not be specific or protective in severe CDI cases. The optimal management must include a low threshold for testing, early recognition, and close monitoring for signs and symptoms of deterioration, such as increased abdominal tenderness and distension, the elevation of leukocyte counts over 20,000/mm<sup>3</sup>, or a rising creatinine level [251]. A subtotal colectomy can be life-saving in severe cases; indications include dilated (>10 cm) intestinal loops, peritonitis, perforation, and persistent sepsis with a leukocytosis of more than 20,000/mm<sup>3</sup> [252].

## 21.2.7 Diagnosis

### 21.2.7.1 Elective Presentation

Diagnostic procedures are no different from usual during pregnancy. Interpretation of blood investigations for IBD during pregnancy can be difficult. Due to hemodilution, hemoglobin and albumin decrease as pregnancy progresses; therefore, they do not help assess disease activity. Iron deficiency is expected from chronic iron loss and could be exacerbated during pregnancy. Therefore, hypochromic, microcytic anemia is frequent. Laboratory investigations include full blood count, urea and electrolytes (potassium, sodium, calcium, and magnesium), liver function tests, erythrocyte sedimentation rate or CRP, ferritin, transferrin saturation, vitamin B12, folate, and albumin.

A proctoscopic examination suggests nonspecific inflammatory bowel disease or shows gross changes characteristic of UC, such as pseudopolyps or ulcerated hemorrhagic mucosa with pus and blood [248]. Biopsy should be taken for definitive diagnosis by pathohistological examination.

The obstetric US is extensively used and is the safest form of radiological imaging. It can assess abscess formation and bowel wall thickness (as

evidence of active inflammation). Also, fetal status is evaluated.

Colonoscopy, flexible and rigid sigmoidoscopy in pregnancy, is safe (see Sect. 21.1.6.3). Also, capsule endoscopy can assess mucosal inflammation in UC [253]. Most manufacturers recommend against its use during pregnancy, while others label pregnancy as a relative contraindication [254]. It is contraindicated in pregnancy because of the microwaves emitted while the capsule is active [255].

### 21.2.7.2 Emergent Presentation

Clinical examination is challenging in the third trimester of pregnancy due to the enlarged gravid uterus and displacement of intraperitoneal organs. During less than 16 weeks of pregnancy, morphology and location of colonic dilation on plain abdominal X-ray are the same as in the non-pregnant population (Fig. 21.9). Specific difficulty during the third trimester is displacement and sometimes distortion of the small and large bowel, making radiologic diagnosis more difficult (Figs. 21.10 and 21.11). Also, it is challeng-



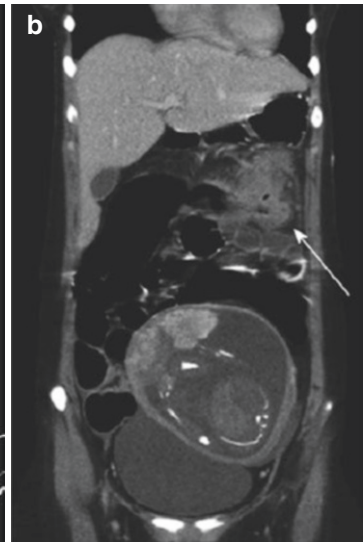
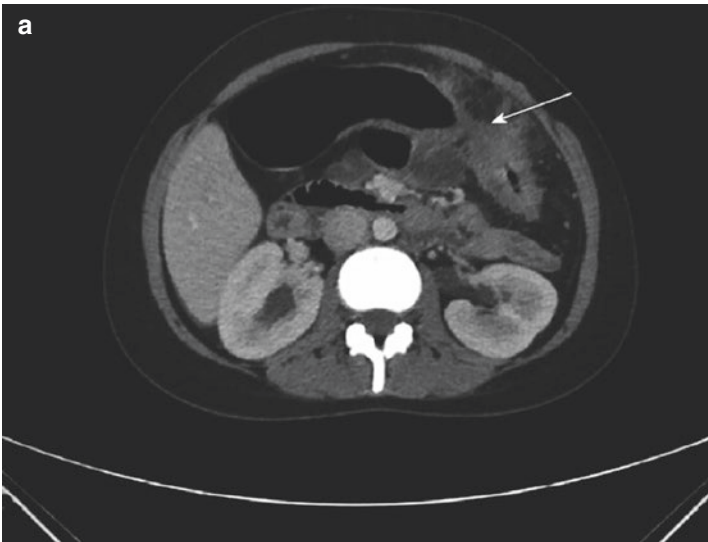
**Fig. 21.9** Plain abdominal X-ray in 16 weeks of gestation shows a persistently dilated transverse colon with a diameter of 8 cm. (Reproduced with permission from [256])



**Fig. 21.10** Supine X-ray in 30 weeks of pregnancy. Gravid uterus displacing gas-filled colon without dilation. (Reproduced with permission from [257])



**Fig. 21.11** Toxic dilation of the colon in the 31 week of pregnancy. Note the progressive bowel displacement as the gravid uterus enlarges (see Fig. 21.10). (Reproduced with permission from [247] under the CC BY Attribution License)



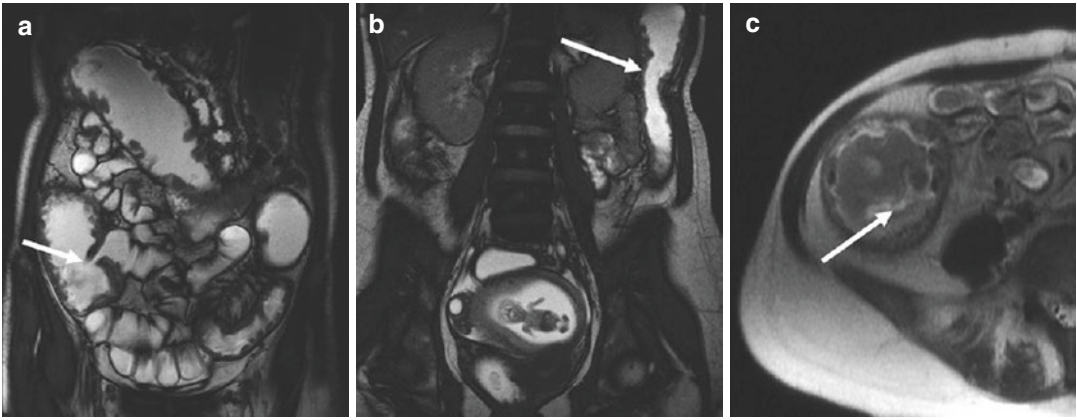
**Fig. 21.12** Abdominal CT at 21 weeks gestation shows (a) the strictured colonic segment near the splenic flexure with proximal dilation (arrow) and (b) adjacent phlegmon (arrow). (Reproduced with permission from [258])

ing to measure colonic dilation in different colonic segments in the third trimester.

In uncertain cases, abdominal CT accurately predicts colonic diameter, ischemic changes,

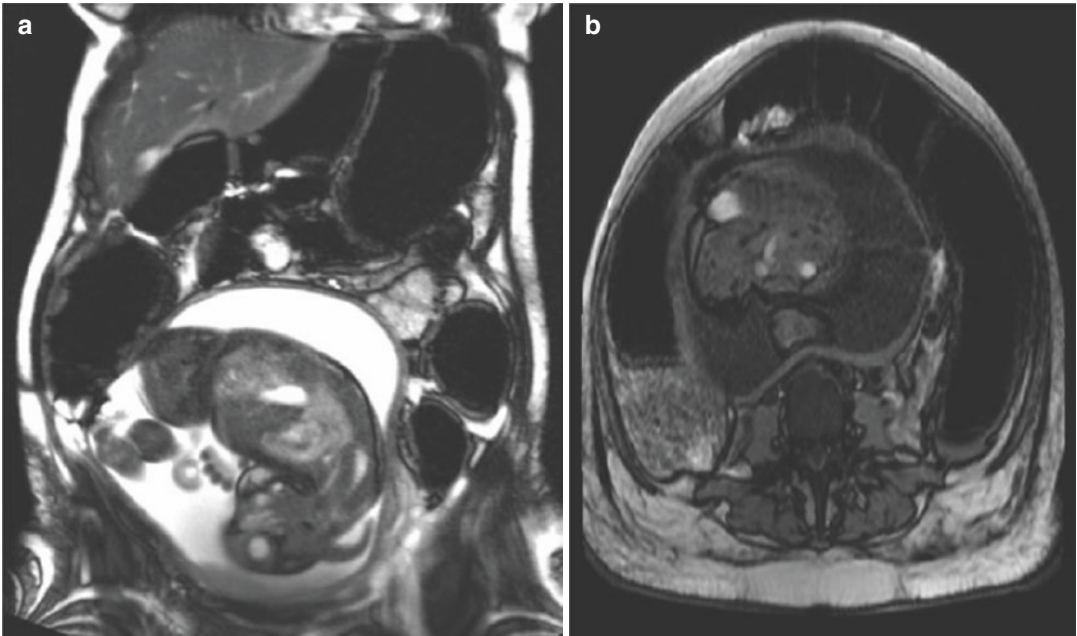
bowel perforation, or stenosis (Fig. 21.12) and determines conservative or surgical therapy [259].

MRI and MRE define (1) the location, (2) the extent of the disease, and (3) can differentiate



**Fig. 21.13** A 11 weeks pregnant patient was diagnosed with UC with a working diagnosis of CD. **(a)** Coronal FIESTA, large bowel mural thickening with a thumb printing pattern

(arrow). **(b)** Coronal FIESTA, ileocecal stenosis (arrow). **(c)** Axial SSFSE T2 submucosal edema (arrow). (Reproduced with permission from [69] under the CC BY 4.0)



**Fig. 21.14** A 11 abdominal MRI for ulcerative colitis at 33 weeks of pregnancy. **(a)** Axial T2 shows a 10-cm gaseous dilation of the entire colon as in toxic megacolon. **(b)** Coronal T1 with evidence of opened fetal hand, i.e., of a

severely compromised fetal muscular tone, suggesting the likelihood of asphyxia. (Reproduced with permission from [260])

between CD and UC, which is especially important in emergent settings when a complete workup is time-consuming (Fig. 21.13). Toxic megacolon can be precisely diagnosed, and fetal compromise can be detected, which helps with obstetric management (Fig. 21.14).

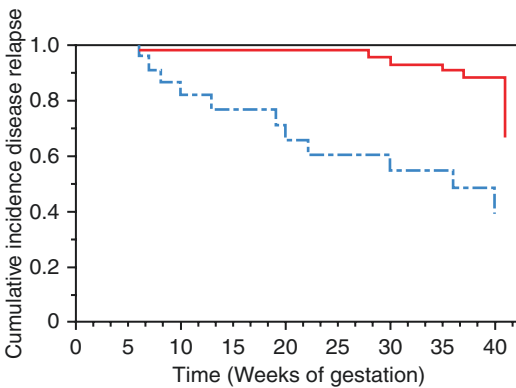
### 21.2.8 Treatment

*Surgery should be avoided if possible during pregnancy. However, each case must be considered individually, and I would hate to increase the risk of the mother's life by postponing indicated surgical intervention just because she is pregnant.*

(John F. Fielding, 1976)

### 21.2.8.1 Conservative Treatment

Non-adherence to medications (<80% intake of the daily prescribed dose) is an independent risk factor for relapse (Fig. 21.15) and possibly for adverse pregnancy outcomes. Among the subgroup treated with oral mesalamine alone, the non-adherence was an independent risk factor for relapse [261]. The rate of non-adherence among pregnant UC women is underestimated (Fig. 21.16). Preconception counseling about the need and safety of medications during pregnancy may help improve adherence.



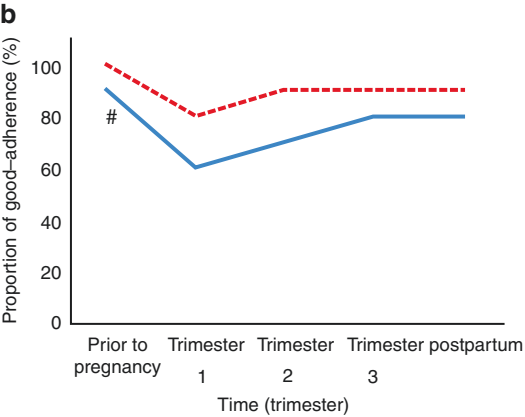
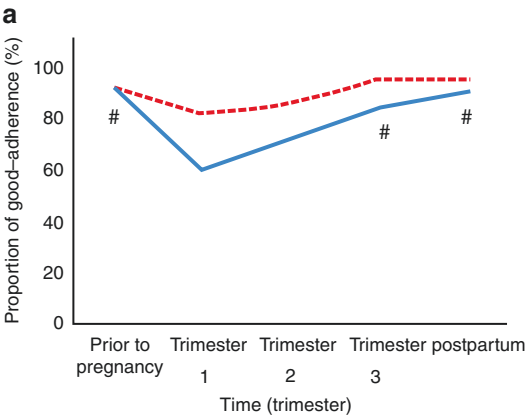
**Fig. 21.15** Comparison of cumulative incidences of UC relapse during pregnancy related to adherence to medical therapy. Those who were non-adherent to their treatment (*dotted line*) had a significantly higher risk of relapse than those with good adherence (*bold line*). (Reproduced with permission from [261])

### 21.2.8.2 Surgical Treatment

During 1940, conservative treatment was common [262, 263]. Surgical treatment had 100% mortality [263]. At that time, an ileostomy was recommended [263]. Although immediate colectomy without medical treatment was advocated for toxic megacolon in pregnancy by Thomas Holzbach in 1969 [231], 24–48 h of intensive medical treatment could be initiated [238, 264–267]. Unfortunately, only 10% responded well to medical treatment (similar to the nongravid state [268]) and gave birth to viable fetuses [238, 266]. Medical treatment of toxic megacolon during pregnancy raises the following issues: (1) the potential effects of drugs on the fetus (see Sect. 21.1.7.1), (2) repeated ionizing imaging, and (3) prolonged inflammation leading to spontaneous abortion or preterm labor.

Early surgery for toxic megacolon due to UC in pregnancy is recommended.

Multiple procedures, from diverting loop ileostomy to total proctocolectomy, treat fulminant and toxic UC in pregnancy. Before the 1950s, an ileostomy was the most commonly performed surgical procedure for toxic megacolon [263]. However, despite the diversion, unsatisfactory results are due to the occasional perforation of



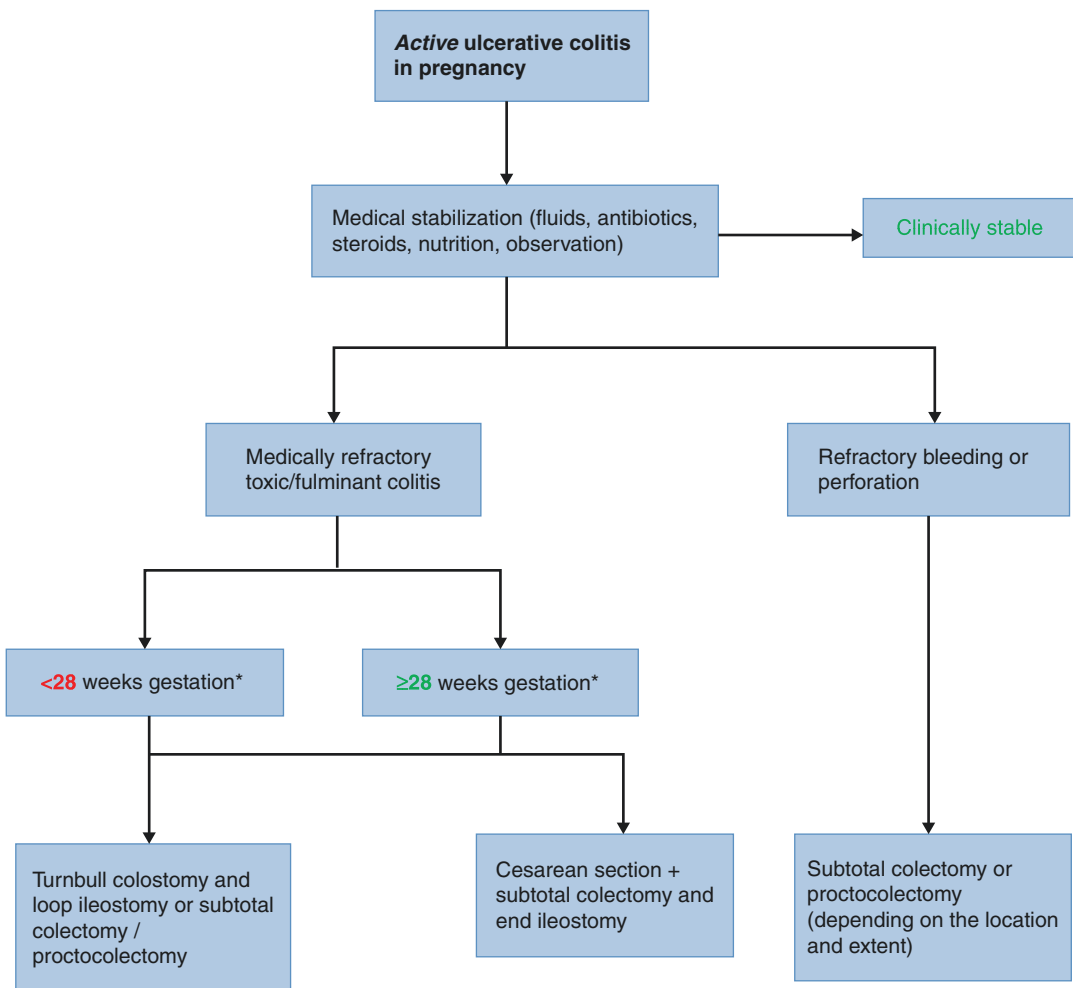
**Fig. 21.16** Proportion of patients self-reporting good adherence (*solid line*), and physician estimated adherence (*dotted line*) with (a) mesalamine and (b) thiopurines. # <0.05. (Reproduced with permission from [261])

the dilated colon. Mortality rates of 50–70% in the general population are similar to medical therapy alone [269]. Proctocolectomy also is inappropriate in the acute situation because it is a long, complex operation and requires pelvic dissection, which may be difficult because of uterine enlargement and grossly dilated pelvic vessels. Moreover, increased manipulation of the gravid uterus increases the risk of spontaneous delivery and preterm labor.

### Indications for Emergent Operation

During the 1980s, 2.3–3.9% of patients with UC during pregnancy required surgical intervention

[238, 270]. Indications for emergent operation are the same as in the general population: intractable bleeding, perforation, toxic colitis (toxic megacolon), and fulminant disease refractory to medical therapy. Gestational age directs obstetric management (Fig. 21.17). Most operations were due to refractory UC or toxic megacolon. The causes of small bowel obstruction were adhesions, small bowel volvulus, or external compression of the gravid uterus on IPAA or small bowel proximal to IPAA [272, 273]. The period to surgery for refractory UC is not defined. However, intra-abdominal sepsis or blood loss from bloody



**Fig. 21.17** Treatment algorithm for pregnant patients with ulcerative colitis. (Modified and reproduced with permission from [12, 271]). \* Due to improvement in neonatal care, CS can be indicated in an earlier pregnancy



stools increases rates of spontaneous abortion, preterm labor, or intrauterine fetal death.

### Turnbull “Blowhole” Procedure

In 1971, Turnbull et al. advised colonic decompression and diversion by blowhole colostomy and loop ileostomy for patients with toxic colon dilation to prevent perforation and sepsis in severely ill patients [274]. The authors recognized the risk of iatrogenic perforation and fecal spillage caused by manipulating the friable edematous colon during colectomy (especially in mobilizing the splenic flexure), which had a high mortality and morbidity rate. The iatrogenic perforation is likely and results in the greater omentum densely adherent to the colon. Occult sealed perforations on the posterior aspect of the colon become overt only when the colon is mobilized. Transmural penetrating ulcers are a feature of toxic dilation of the colon and are “plugged” or sealed on their serosal aspect by the omentum or adjacent viscera. Disrupting these seals results in fecal spillage. To avoid colon manipulation, colonic decompression and diversion in the form of a skin-level (“blowhole”) colostomy and loop ileostomy are advised (Fig. 21.18). Contraindication includes free perforation, abscess, and bleeding. However, the large size of their uterus and minimal manipulation, rather than the severity of the UC, is sometimes the deciding factor for the blowhole procedure [256].

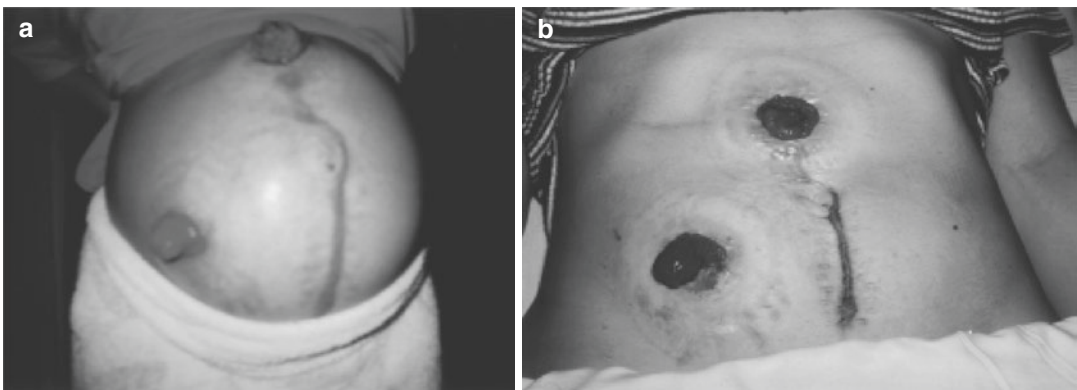
Otherwise, these patients are candidates for (sub) total colectomy and ileostomy.

This procedure has the advantage of short anesthesia time and minimal surgical trauma, which may dramatically improve outcomes in extremely ill patients. The disadvantage of a blowhole colostomy is that the remaining colon may cause ongoing toxicity (severe bleeding, sepsis), requiring repeat operation, leading to increased risk to the mother and fetus. Therefore, the Turnbull “blowhole” procedure is far less practiced currently. If performed, definitive surgery is completed after delivery.

IPAA can be successfully performed after delivery in all patients undergoing Turnbull blowhole colostomy or (sub)total colectomy during pregnancy [275].

### Subtotal and Total Colectomy

In 1951, Crile and Thomas advised total abdominal colectomy with Brooke end ileostomy to preserve the rectum due to toxic megacolon [276]. This is the most commonly performed procedure for severely ill patients who require urgent or emergent colectomy for fulminant or toxic UC. It eradicates most of the disease and requires no bowel anastomosis or deep pelvic dissection while allowing the



**Fig. 21.18** (a) Gravid patient with healed midline scar, loop ileostomy (to the right of the midline), and skin-level transverse colostomy. (b) The same patient after elective

cesarean section. A scaphoid abdomen with transverse colostomy and ileostomy, ready for restorative proctocolectomy. (Reproduced with permission from [256])

patient to be weaned from most medical agents. Also, it does not preclude or compromise the results of subsequent IPAA [160, 277]. After colectomy, a decision should be made regarding the rectal stump. Stump breakdown and leakage lead to intra-abdominal sepsis. The stump can be handsewn in two layers and wrapped with the greater omentum, and this is a safe procedure if the inflammatory process has not compromised the integrity of the bowel wall. Another option is to bring out the rectal stump as a mucus fistula. Because of the enlarged uterus, the stump will need to be brought out through an extraperitoneal plane deep into the broad ligament and dilated ovarian vessels. In advanced pregnancy bringing out the distal sigmoid colon as a mucous fistula would be hindered by the broad ligaments draped across the abdominal cavity from the enlarged uterus [278]. Therefore, Hartmann's procedure with the short rectal stump is an alternative. The rectum is irrigated with anti-septic solutions during surgery to remove the excess bloody mucoid material, and a rectal tube keeps it decompressed postoperatively [160].

Rectal excision, when indicated, for example, in intractable rectal bleeding, may be complicated by the need for hysterectomy. This is because the injury of the engorged pelvic veins leads to severe bleeding.

A stomal therapist should mark potential stoma locations before surgery.

In pregnant patients, the optimal location for the stoma on the abdominal wall is usually cranial because the stoma will drop to a lower position after delivery (Fig. 21.18).

### Synchronous Cesarean Section and Surgery

Most pregnant women requiring urgent surgery for UC have undergone metachronous colonic surgery and CS or vaginal delivery with high maternal and fetal morbidity and mortality. Four cases have been reported with synchronous col-

ectomy and delivery, two at 32 weeks, one at 28 weeks, and one at 23/3 weeks gestation without maternal or neonatal morbidity or mortality [265, 271, 279, 280]. Also, in previously operated UC patients, other intestinal operations, depending on the cause of acute abdomen (adhesiolysis, volvulus), with indicated CS, an intestinal operation is performed [275].

#### 21.2.8.3 Therapeutic Abortion/Delivery

Up to 1951, the risk to the mother was considered so high that therapeutic abortion was advocated if severely active UC occurred during pregnancy [18], based on the positive effect of delivery or miscarriage on the disease activity [237, 262]. In 1971, the therapeutic abortion for the treatment of UC was questioned [193].

#### 21.2.8.4 Obstetric Management

##### Mode of Delivery

Recommendations for CS are as follows:

- Acute abdomen in the late third trimester,
- IPAA,
- Bowel or IPAA obstruction with a gravid uterus,
- Acute or chronic pouchitis.

Treatment of acute abdomen depends on the trimester of pregnancy. During the first two trimesters, only surgical treatment of the cause of the acute abdomen is made. In the late third trimester, due to the high incidence of postoperative (during the first few days) spontaneous inductions of labor, CS is recommended [160, 179]. After surgery without CS, fetal monitoring starts in the postanesthesia recovery room to detect spontaneous labor.

IPAA alters the anatomy of the gastrointestinal tract, placing the pouch at risk from compressive obstruction by the gravid uterus. Induction of labor in a near-term fetus is a reasonable initial management method, preventing external com-

pression on the IPAA and small bowel obstruction [273]. Patients with IPAA can have a normal vaginal delivery without fears of damaging the pouch or fissuring the anal sphincter [281, 282]. Subclinical differences in anorectal physiology are demonstrated as women with vaginal deliveries had significantly lower squeeze pressure on anorectal manometry and significantly more anal sphincter defects detected by the anorectal US than those with CS [171]. In general, anal sphincter function (daytime and nighttime stool frequency or continence) may be altered during the third trimester and immediate postpartum period. However, its function typically returns to baseline in most patients, usually within 3 months after delivery [170, 281–283]. Although a few patients may have long-term disturbances in anal function, it appears unrelated to the method of delivery [283]. Damage to the anal sphincter may be compounded by aging, and the effects on the pouch will not be seen for several years. Functional IPAA outcomes with vaginal deliveries after IPAA were no different from those of women who did not have children after IPAA [284]. There is one case of successful decompression of IPAA compression by gravid uterus by emergent CS. The obstruction was proximal to IPAA [272].

There is no mention of the type of delivery when pouchitis is present. The patient, the obstetrician, and the surgeon should discuss the theoretical risk to long-term pouch function depending on the mode of delivery.

Although the first report led to the recommendation of CS to avoid damage to the sphincter mechanism [285], later reports stated that most pregnant women with an IPAA could deliver vaginally with episiotomies [168, 169]. In some cases, the technique of episiotomy had to be modified to a mediolateral position [248]. A cohort of 72% of colorectal surgeons believed they should advise the patient on the optimal mode of delivery and not the obstetrician or the gastroenterologist [286]. Established risks of vaginal delivery, such as pouch and sphincter injury, may result in fecal incontinence [167, 168, 170, 171, 287]. These concerns account for colorectal surgeons' higher preference for CS

(62%) [286]. However, this may be an unfounded concern that can lead to unnecessary recommendations for CS [170, 283, 288]. The national average for CS in general in the USA, independent of specific maternal medical issues, is already 32%. The unnecessarily increasing CS rate places IPAA patients at a higher risk of complications associated with repeat CS [289]. CS has inherent risks [167, 283], and measures have been undertaken to decrease the rates of the first CS.

### 21.2.9 Prognosis

Early reports emphasized that the onset or exacerbation of symptoms during pregnancy was frequently fatal to both mother and baby [263]. The preexisting renal disease probably played a large part in the poor prognosis.

The disease severity at conception plays a major role in the outcome. The ideal timing for patients who want to conceive is UC in remission.

There is a significantly higher rate of gestational diabetes among UC patients using ART than CD patients (29.4% vs. 6.1%) [178].

#### 21.2.9.1 Maternal Outcome

##### Mortality

Maternal mortality depends on the decade of presentation, the severity of UC, and the type and extent of UC that indicates emergent operation. During the 1940s, patients were mostly treated conservatively [262, 263], and subgroups needing emergent operation had 100% mortality [263]. Up to 1951, if the first episode started during pregnancy, the mortality was 80% [18]. In 1971, maternal mortality with medical treatment was 0%, while it was 20% in the surgically treated group [93]. In medically refractory UC, as for fetal mortality, maternal mortality can be arbitrarily divided into periods

before 1987 and after. Before 1987, the maternal mortality rate was 26–29% (all deaths until 1972), while after 1987, it was 0% [12, 267]. With toxic megacolon during pregnancy up to 1972, maternal mortality in cases with available data was 36% [266].

### Breastfeeding

Breastfeeding may protect against the development of IBD in infants, with a pooled odds ratio of 0.56 (0.38–0.81) for UC [210]. However, these were not mothers who had IBD themselves. Breastfeeding is recommended for at least 6 months after birth (see Sect. 21.1.8.2).

### Fertility and Sexual Health

Relationships, sexual health, and fertility in IBD patients are interrelated. UC does not affect fertility [20, 97, 235, 236, 239, 270, 290]. Other studies that found reduced fertility was probably flawed owing to short follow-up periods, patient selection, and inadequate medical control of the disease [237, 291] or inadequate numbers of patients observed [292]. Therefore, women with UC have fertility rates similar to the general population before surgery [97, 202, 203].

While some reported no difference in fertility rates post-IPAA [203, 287], others showed a significant decrease in fertility rates (by as much as 80%) [293]. There is a threefold increase in infertility after an IPAA [294], with 38.6–48% of infertility in UC patients after IPAA versus 13.3–15% in UC patients managed nonoperatively [295, 296]. Proctocolectomy with ileostomy reduces fertility [297], as do patients with familial adenomatous polyposis who undergo IPAA [298]. The risk of infertility after IPAA should be discussed with the patient before surgery. Most likely, the greatest reduction in fertility results from (1) extensive pelvic dissection involved in creating the pouch, (2) the consequent adhesion formation in the pelvis causing fallopian tube scarring and occlusion, and (3) direct damage to the reproductive organs. Although not proven, some recommend encircling the ovaries and tubes with anti-adhesion membranes at the time may reduce the incidence of peritubal adhesions [299], potentially improving fertility. A potential

option for some patients may be an ileorectal anastomosis, which preserves fertility [300]. It is unclear if subtotal colectomy with rectal stump and ileostomy during the childbearing years and then creating an IPAA later in life reduces infertility rates. The drawbacks of the latter procedure include rare ileostomy complications during pregnancy, such as obstruction and stoma-related problems [301], technical difficulties in creating a functioning pouch several years after the initial surgery, and the patient's reluctance to have a long-term ostomy. The total laparoscopic colectomy with IPAA causes significantly lower infertility rates than the open approach [299, 302, 303]. IPAA does not appear to impact IVF success rates [304]. IPAA failure impairs the birth rate by 50%. The success of IVF was not significantly different in nonfailures and UC women. However, the success was significantly lower in the IPAA group compared with UC women [305]. IPAA failure results in inflammation within the pelvic cavity and additional surgery, which might further decrease fertility. Voluntary infertility is probably also part of the problem because the incidence of IVF treatment is not increased in female pouch failures compared with nonfailures. However, the birth rate is significantly lower in female pouch failures.

“Easier” decision is when an acute abdomen indicates an emergent operation. With a life-saving operation, fertility is the third goal after maternal and fetal survival. Half of the operated patients for toxic megacolon developed severe postoperative pelvic and subphrenic abscesses. 3/4 of patients had difficulty conceiving or developed secondary infertility. The social morbidity was the high divorce rate (3/4) [267]. Despite these problems encountered during pregnancies, it is interesting that each of these patients has tried (and two have succeeded) to become pregnant again, albeit generally by a different husband.

In conclusion, In UC, overall fertility rates are normal [294, 306] except after surgical resection with IPAA [288, 293, 296, 307]. The estimated risk of infertility after IPAA is three times higher [295]. Colectomy with ileorectal anastomosis [300] or subtotal colectomy with an ileostomy during pregnancy and IPAA after childbearing

[137] may be reasonable alternatives for women wishing to become pregnant [137, 308]. Laparoscopic IPAA could reduce adhesions and is a suitable alternative for patients of childbearing age [299, 302, 303]. The patients with IPAA in pregnancy have a small increase in nocturnal stool frequency [168, 248].

### 21.2.9.2 Perinatal Outcome

#### Mortality

Perinatal mortality depends on the decade of presentation and the type of UC pathology that indicates emergent operation. Up to 1971, in medically treated patients, the abortion rate was 8%, and the perinatal mortality rate was 2%, below the national estimates [93, 237]. In the surgically treated group, fetal mortality (abortion + stillbirth) was 60% [93].

In medically refractory UC, fetal mortality can be arbitrarily divided into periods before 1987 and after. Before 1987, the fetal mortality rate was 58%, while after 1987, it was 0% [12]. In all reported cases, surgery in the third trimester resulted in preterm labor. Generally, there were 50% of preterm births [12]. Until 1972, fetal mortality for maternal toxic megacolon was 100% [266]. Until 1986, it declined to 50% [18, 93, 231, 264–267, 270, 279, 309–313]. Recently, fetal mortality has approached 0% [275]. The declining but present stillbirth rate probably reflects the severity of the disease rather than the effects of the operation. Similar to maternal outcomes, better fetal outcomes result from advances in surgery, perioperative care, perioperative nutrition, and neonatal care.

#### Morbidity

Today, completed pregnancies result in 84% of healthy term babies and 77% in uncomplicated vaginal deliveries. Low birth weight and post-maturity are not more common than usual. Even when UC first developed during pregnancy, there was a good chance (88%) of normal live birth [97]. In contrast to CD, women with UC had similar rates to controls of preterm delivery, LBW, and small for gestational age infants but a signifi-

cantly higher rate of congenital malformations (7.9% vs. 1.7%) [314]. The study did not account for medication use, and the results have not been replicated in other studies. The studies that reported on congenital abnormalities did not distinguish between major and minor malformations; one study included chromosomal disorders [314], which may result in an overestimated risk. The *Hungarian Case Control Surveillance* of congenital anomalies (1980–1996) reported a 1.3× higher risk of congenital anomalies in UC patients than controls and adjusted for parity, age, and medication use [315]. A meta-analysis showed a normal pregnancy in 76–87% of patients. Fetal malformations were observed in 1% of pregnancies, and the frequency of spontaneous abortions and stillbirths was similar to that observed in the general population [219].

Predictors of poor outcomes (preterm birth, LBW, intrauterine growth retardation, small for gestational age, congenital anomalies, APGAR scores, stillbirth, and labor complications) were significantly higher having UC and having surgery for UC [187]. In the studies from the 1980s, disease activity at conception was associated with a higher rate of fetal loss [29] and preterm birth [87]; disease activity during pregnancy was associated with LBW and preterm birth [10, 162, 188, 189]. One hypothesis is that an increase in circulating prostaglandin levels during a flare could initiate preterm labor with the induction of smooth muscle contraction [192, 193]. Another theory is that increased gut permeability during increased inflammation could alter nutritional and immunological factors affecting labor [192].

Conversely to CD, smoking in UC women does not increase their risk of preterm delivery [279]. However, smoking cessation should be encouraged, given the known risk of smoking to the individual and the baby.

Women with UC have 1.5× the risk of fetal central nervous system defects [213]; the association is not related to whether UC occurred before or after delivery or whether a conception was before or after 2000 when the biologics and folic acid food fortification were introduced [213].



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# Gastrointestinal Perforation or Rupture

# 22

## Abstract

Gastrointestinal perforations of the upper gastrointestinal tract are extremely rare. Peptic ulcer symptoms decrease during pregnancy due to healthier maternal habits during pregnancy and pregnancy-induced hormonal gastroprotection. The maternal outcome is excellent, while fetal mortality increases with the duration before surgical intervention. On the contrary, perforations of the lower intestinal tract are more common due to spontaneous, disease-induced, and postinterventional perforations. Aside from intestinal endometriosis-induced perforations, the most common are postinstrumental perforations for the termination of pregnancy. This is seen as transuterine bowel perforation and is more common in undeveloped and developing countries where illegal abortion is relatively frequent. It is a complex injury necessitating simultaneous obstetric and surgical management. Extension of bowel injury determines maternal outcome and quality of life.

## 22.1 Perforated Peptic Ulcer

### 22.1.1 Peptic Ulcer in Pregnancy

*I have never seen undue activity of a peptic ulcer during pregnancy, but I am very familiar with the opposite state of affairs where ulcer symptoms disappear during pregnancy.*

(George Grey Turner)

#### 22.1.1.1 Incidence

Reports from the twentieth century have variable incidence, although the incidence is very low. Cappell and Sidhom reported that 0.19% of hospitalized pregnant patients had severe upper gastrointestinal complaints [1]. Only 2/20 women undergoing esophagogastroduodenoscopy (EGD) had PUD (specifically duodenal ulcers). Tests to evaluate suspected PUD (e.g., upper gastrointestinal series or EGD), routine in the general population, have been conservatively performed on pregnant women [2]. At the Central Middlesex Hospital, London, during the 11 years (1951–

1961), the incidence of the duodenal ulcer was 1/11, 497 confinements; the same incidence of 1/11, 497 confinements was for gastric ulcers and simultaneous peptic ulceration and bleeding (with additional dyspepsia in three and gastritis in three) patients [3]. Sandweiss et al. [4] found PUD in 1/70, 310 pregnancies, Johnston [5] in 1/6021, and Durst and Klieger [6] in 1/24, 915. In England and Wales (1951–1960), 0.58% of all deaths associated with pregnancy were from PUD [7], while 0.3% of all deaths in women aged 20–49 were due to PUD [8]. Duodenal ulcers in early pregnancy are extremely rare (see Sect. 22.1.1.3). During 15 years, five cases were published [9, 10].

On the contrary, there is a higher incidence of maternal dyspepsia during pregnancy than in the general population. Dyspepsia is among the most common gastrointestinal diagnoses and is estimated to occur in 14–20% of adults [11, 12]. Dyspepsia is a common symptom in pregnancy, particularly in the second part, when 21% of pregnant women complain of heartburn daily, 52% at least once a month, and 80% in the third trimester [13, 14].

### 22.1.1.2 Pathophysiology

Pregnancy has a beneficial effect on PUD. The remission of PUD symptoms in pregnancy is related to the general feeling of well-being, success, and fulfillment characteristic of that state. At the same time, the mental stresses, irritability, and emotional imbalance of menopause may account for renewed ulcer activity. Pregnancy is a period of increased hormonal activity with a marked increase in the gonadotrophic, luteal, and estrogenic hormones.

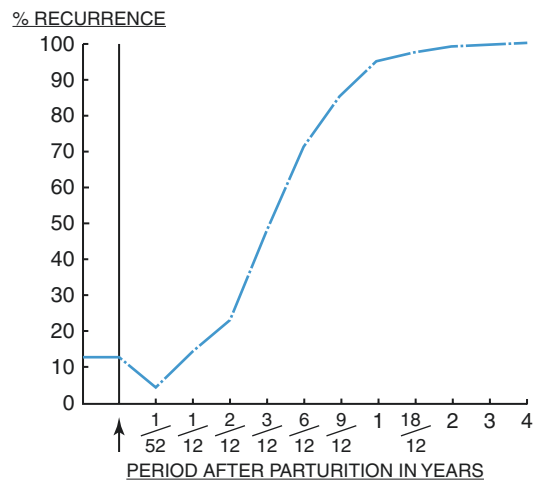
Dyspeptic symptoms usually disappear about the end of the third month of pregnancy, but they may persist till the term. The estrogen level and the greatly elevated histaminase concentration explain why symptoms and complications of PUD are so rare during pregnancy. Occasionally, more severe indigestion occurs with a considerable resemblance to a PUD. Sandweiss et al., in 1939, reported that in almost all cases, PUD symptoms disappeared during pregnancy [15]. Clark, in 1953, confirmed a remission of PUD symptoms in 88% of pregnant patients with a

symptomatic prepregnancy PUD. With prepregnancy PUD, 44.8% became asymptomatic during pregnancy, 43.4% improved, and only 11.8% failed to improve during pregnancy. Bleeding or perforation never occurred during the pregnancy [16]. The benefits from pregnancy in women with PUD are short-lived, with almost 100% recurrence within 2 years postpartum (Fig. 22.1).

In almost 90% of prepregnancy PUD, symptoms disappear during pregnancy. After parturition, the recurrence is common, mostly during the first two postpartum years [16].

### Gastric Position Changes

Arthur F. Hurst and Matthew J Stewart, in 1929, stated that pregnancy exerts a favorable influence on the symptoms of a PUD and, in some cases, appears to lead to actual healing apart from any specific treatment. This they attributed to the mechanical effects of support of the stomach by the rising uterus. This is supposed to relieve the strain on the lesser curvature and improve the local circulation, promoting the healing of the ulcer [17]. In several cases [18, 19], major accidents occurred when the stomach could not have



**Fig. 22.1** Recurrence of peptic ulcer symptoms after parturition. (Reproduced with permission from [16])

been lifted much higher in advanced pregnancy. Therefore, the mechanical theory by Hurst and Stewart is questionable.

### Hypochlorhydria

In 1927, Balint [20] first suggested a general tendency toward increased alkalinity in tissue fluids during pregnancy. Other observers have confirmed that a hypo- or achlorhydria is present with increased alkalinity, especially in the first 6 months of pregnancy. After that, the acid values rise toward normal or supranormal values in the puerperium [21–23]. Nakai's earliest observation of gastric acidity in pregnancy was in 1925, when he showed a striking diminution in both the free and total acid contents of gastric juice in response to a test meal [21]. This was confirmed by Artz [23], who noted that the lowest secretion of free acid coincides with the period of pregnancy when nausea and vomiting are common. Murray et al. noted with the maximal histamine test that maximal secretion was decreased in the first 30 weeks of pregnancy [24]. This decreased secretion could be due to several factors. Plasma diamine oxidase (histaminase) levels are markedly increased in pregnancy [25], and there is evidence from the 1960s that this substance is related to gastric secretion and may inhibit it [26]. Another important observation is that regurgitation of duodenal contents, especially bile, is present in only 3% of pregnant patients despite common nausea and vomiting during (early) pregnancy [22, 27]. The authors believe that duodenal regurgitation is not the cause of hypochlorhydria.

### Hormones

Burrill Bernard Crohn in 1927 [28], Robert Mussey [29], and others noted that PUD tends to break down in the puerperium. Winkelstein (1940) thought that the agent responsible for the breakdown might be prolactin. During gestation, the formation of prolactin is inhibited by the high blood levels of ovarian and placental hormones. He made experimental studies on animals with chemically produced PUD by treating them with the ovarian hormone theelin. The response was good, and the ulcers healed within 10 days.

The maximal levels of chorionic gonadotropins also correspond to the period of decreased gastric secretion. The increased estrogen level may be a factor, with a beneficial effect of stilbestrol on duodenal ulcers [30]. The equal sex incidence of PUD in children, the decreased incidence in women during the childbearing years, and the increased incidence at the time of menopause [31] suggest that the female sex hormones are related to PUD and that the alterations in the hormones during pregnancy may give rise to increased resistance to PUD. Duodenal ulceration and its complications with high blood levels of estrogens and progestagens must be due to factors other than changes in acid output. Protection against gastric ulceration during pregnancy in rats with raised acid output has been observed [32].

Plasma pepsinogen rises in the last trimester of pregnancy, reaching a maximum on the first postpartum day [33]. There is a decreased secretory response to histamine acid phosphate during pregnancy, mainly during the first 30 weeks [24]. Two possible explanations for diminished hydrochloric acid secretion have been offered. The first is the antisecretory effect of plasma histaminase, which increases in pregnancy up to 1000-fold [34]. Plasma histaminase begins to rise about 7 weeks of pregnancy, while the peak is reached in the 26th–28th weeks of gestation [25]. An increase in plasma histamine in pregnancy (caused by placental histaminase synthesis) increases the metabolism of maternal histamine, thereby reducing gastric acid secretion during pregnancy [25].

Way, in 1945, attempted to explain the rarity of PUD and complications in pregnancy by correlating the hypochlorhydria with the increased secretion of the anterior pituitary-like hormones in the urine. The greater the secretion of this latter, the more marked the hypochlorhydria. This endocrine explanation appears to be the most likely reason for the rarity of PUD activity during pregnancy [27, 35]. Hormonal changes characterized by significant increases in 17-hydroxysteroids and 17-ketosteroids are a potential factor in PUD in late pregnancy [35]. These and other observations suggest that estrogens may protect

against PUD. This concept was supported in 1960 by the beneficial effect demonstrated when stilbestrol was used to treat men with duodenal ulcers [36].

Female gestational hormones (progesterone in particular) decrease the rate of PUD formation by increasing gastric mucus synthesis. Progesterone protects the gastroduodenal mucosa against ulcerogenic cysteamine or indomethacin [37].

### Fertility Rate and Peptic Ulcer

One of the causes of the rarity of PUD in pregnancy is that patients with duodenal ulcers, regardless of sex, have a 25% lower fertility rate than the general population (at least in the era before assisted reproduction) [38]. PUD reduces reproductive ability because the number of children born to affected probands and affected parents is smaller than that of unaffected individuals. The finding was supported by the number of children of patients with PUD was not influenced (i.e., further reduced) by a positive family history of PUD. By contrast, detailed analysis revealed that childlessness was more frequent in affected probands with a positive family history of PUD than in affected probands with a negative family history: 26% compared to 16%, respectively. Positive family history increases the rate of childless marriages for subjects suffering from PUD. At the same time, it has no bearing on the number of children born. However, the number is reduced compared to the average for the general population due to the proband's disease.

There is a possibility that PUD and reduced fertility rates are not directly bonded. In 1939, 46.7% of women with PUD showed pituitary, thyroid, or gonadal abnormalities [39]. During the first half of the twentieth century, it was stated that female patients with PUD should be checked for endocrine abnormalities that could be (partly) responsible for the reduced fertility rate.

#### 22.1.1.3 Risk Factors

All known risk factors for PUD in the general population are also risk factors in the pregnant population.

### *Helicobacter pylori* Infection

See Sect. 22.1.1.8.

### Medications

*NSAID* use is a common cause of PUD. These drugs disrupt the mucosal permeability barrier, rendering the mucosa vulnerable to injury. Around 30% of adults taking NSAIDs have adverse GI effects. Factors associated with an increased risk of duodenal ulcers in the setting of NSAID use include the history of previous PUD, advanced age, female sex, high doses or combinations of NSAIDs, long-term NSAID use, concomitant use of anticoagulants, and severe comorbid illnesses. Although the idea was initially controversial, most evidence supports the assertion that *H. pylori* and NSAIDs are synergistic for developing PUD. *H. pylori* eradication in NSAID-naïve users before starting NSAIDs is associated with a decrease in PUD [40].

*Corticosteroids* alone do not increase the risk for PUD; however, they can potentiate PUD risk in patients who use NSAIDs concurrently.

### Lifestyle Factors

Evidence that *tobacco* use is a risk factor for duodenal ulcers is inconclusive. Support for the pathogenic role of smoking comes from the finding that smoking may accelerate gastric emptying and decrease pancreatic bicarbonate production. Studies have produced contradictory findings. Smoking is harmful to the gastroduodenal mucosa, and *H. pylori* infiltration is denser in the gastric antrum of smokers [41].

*Ethanol* is known to cause gastric mucosal irritation and nonspecific gastritis. Evidence that the consumption of alcohol is a risk factor for duodenal ulcers is inconclusive.

Little evidence suggests that *caffeine* intake increases the risk of duodenal ulcers.

### Severe Physiological Stress

Stressful conditions that may cause PUD include burns, CNS trauma, surgery, and severe medical illness. Serious systemic illness, sepsis, hypotension, respiratory failure, and multiple traumatic injuries increase the risk for secondary (stress) ulceration. Cushing ulcers are associated with a

brain tumor or injury and are typically single, deep ulcers prone to perforation. They are associated with high gastric acid output and are located in the duodenum or stomach. Extensive burns are associated with Curling ulcers. Severe illness and decreased gastric pH are related to an increased risk of gastric ulceration and bleeding.

**Hypersecretory States**

The following uncommon hypersecretory states may cause PUD:

- Gastrinoma (Zollinger–Ellison syndrome) or multiple endocrine neoplasia type I,
- Antral G-cell hyperplasia,
- Systemic mastocytosis,
- Basophilic leukemias,
- Cystic fibrosis,
- Short bowel syndrome,
- Hyperparathyroidism.

**Fasting (General Population)**

The frequency of PUD in the general population increases during Ramadan, and PUD complications are more frequent during Ramadan than before and after Ramadan [42]. There is one case of duodenal PPU during Ramadan in pregnancy [43].

**Additional Risk Factors**

Other risk factors associated with PUD are listed in Table 22.1.

**22.1.1.4 Clinical Presentation**

PUD is rare and difficult to diagnose during pregnancy. The beneficial influence of pregnancy on PUD symptoms was confirmed in 1903 by Chabannes [44]. Obstetric patients are not questioned closely about past gastrointestinal symptoms. Epigastric distress, heartburn, nausea, and vomiting are frequent complaints during normal pregnancy and, therefore, often overlooked. These symptoms are also associated with hyperemesis gravidarum and hiatal hernia, both more prevalent than PUD in pregnancy. Dyspepsia is common in pregnancy, particularly in the second part, when 21% of pregnant women complain of heartburn daily, 52% at least once a month, and as many as 80% in the third trimester [13, 14].

**Table 22.1** Less common causes of peptic ulcer disease in the general population

|                                                                                                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Hepatic cirrhosis                                                                                                                                                                         |
| Chronic obstructive pulmonary disease                                                                                                                                                     |
| Allergic gastritis and eosinophilic gastritis                                                                                                                                             |
| Cytomegalovirus infection                                                                                                                                                                 |
| Graft-versus-host disease                                                                                                                                                                 |
| Uremic gastropathy                                                                                                                                                                        |
| Henoch–Schönlein gastritis                                                                                                                                                                |
| Corrosive gastropathy                                                                                                                                                                     |
| Celiac disease                                                                                                                                                                            |
| Bile gastropathy                                                                                                                                                                          |
| Autoimmune disease                                                                                                                                                                        |
| Crohn’s disease                                                                                                                                                                           |
| Other granulomatous gastritis (e.g., sarcoidosis, histiocytosis X, and tuberculosis)                                                                                                      |
| Phlegmonous gastritis and emphysematous gastritis                                                                                                                                         |
| Other infections (Epstein–Barr virus, HIV, <i>Helicobacter heilmannii</i> , herpes simplex, influenza, syphilis, <i>Candida albicans</i> , histoplasmosis, mucormycosis, and anisakiasis) |
| Chemotherapeutic agents, such as 5-fluorouracil (5-FU), methotrexate (MTX), and cyclophosphamide                                                                                          |
| Local radiation resulting in mucosal damage                                                                                                                                               |
| Cocaine, which causes localized vasoconstriction                                                                                                                                          |

The onset of PUD is before conception in most pregnant women but continues during pregnancy; therefore, these women have chronic PUD. However, more than 60% of pregnant women with PUD had the onset after the third gestational month. PUD was more frequent in older multiparous pregnant women, while pregnant women with PUD were not older than the reference sample [45].

Cardinal symptoms of PUD are upper abdominal pain, nausea, and vomiting. The pain is often epigastric and worse at night. In the presence of a gravid uterus (especially when labor ensues), it can be difficult for patients to localize pain. Unlike gastroesophageal reflux disease, the pain is not exacerbated by recumbency or associated with regurgitation. Although nausea and vomiting occur in 50–80% of normal pregnancies, it is uncommon for these symptoms to persist beyond 20 weeks of gestation. Nausea and vomiting of pregnancy are most intense in the morning, while PUD symptoms are worse nocturnally and postprandially. PUD symptoms also get worse with increasing gestation and are usually most severe in the third trimester. Occasionally, PUD may present with hematemesis.



Uncomplicated PUD produces minimal physical signs. The symptoms of PUD mostly improve during pregnancy. Relief occurs early in pregnancy, but unfortunately, the symptoms frequently recur following delivery (Fig. 22.1) [18].

### 22.1.1.5 Diagnosis

Diagnostic modalities are the same for the pregnant and general populations. The most common diagnostic tool during the nonemergent presentation is EGD. It can obtain samples for histopathological examination and *H. pylori* presence. The procedure is safe during pregnancy if no sedative medications are used, which can lead to fetal hypoxia [46]. *American Society for Gastrointestinal Endoscopy* (ASGE) guidelines state two indications for EGD:

- Significant or continued GI bleeding,
- Severe or refractory nausea and vomiting or abdominal pain.

Therefore, if only uncomplicated PUD is suspected, there is no need for endoscopy during pregnancy, or it should be postponed until the second trimester [47].

### 22.1.1.6 Treatment

Pharmacological treatment is the same in the pregnant and general population (see Sect. 22.1.2.5). All classes of medications are safe for the fetus without increasing fetal anomaly rates [45]. No severe side effects were observed in any of the mothers or their newborns. No malfunctions or malformations were observed in the newborns. Follow-up of the children between 2 and 12 years showed normal development in all children [48]. A higher rate of congenital anomalies was not found in the offspring of mothers with PUD [45]. One study showed the possible risk of isolated rectal/anal atresia/stenosis [49].

### 22.1.1.7 Prognosis

#### Maternal Outcome

PUD does not influence maternal mortality and morbidity. Only perforation increases maternal mortality and morbidity (see Sect. 22.1.2.6).

#### Fetal Outcome

Maternal PUD is independently associated with a 1.18-, 1.20-, and 1.25-fold increased risk of neonatal low birth weight, preterm delivery, and small for gestational age, respectively, after adjusting for family income and maternal, paternal, and infant characteristics.

In comparing the PUD women without treatment to unaffected mothers, gestational PUD has adverse pregnancy outcomes. Glucose, transmitted from the mother to the fetus, is the primary energy substrate for intrauterine growth [50]. Whereas glucose is produced by maternal metabolism, dietary restriction or maternal hypoglycemia decreases metabolic fuel availability and consequently slows fetal growth [51, 52]. In response to symptoms of anorexia, abdominal distention, epigastric pain, and postprandial vomiting, mothers with PUD during pregnancy may restrict their dietary intake to avoid discomfort. The risk of constrained fetal growth and adverse birth outcomes might be elevated accordingly.

Stress might also contribute to the link between gestational PUD and adverse pregnancy outcomes. Stress is strongly associated with PUD because threats to homeostasis prompt an adaptive or allostatic response [53]. Maternal vasoconstriction from the release of catecholamines in exposure to stress might obstruct the transmission of oxygen and vital nutrients to the fetus [54]. The fetal central nervous system, particularly glucocorticoid brain receptor development, might subsequently be affected [55]. A significant relationship was demonstrated between maternal prenatal stress and infants with low birth weights and decreased gestational age [55]. Thus, women with PUD might perceive or experience more stressful circumstances.

Furthermore, there is an increased risk of adverse pregnancy outcomes among mothers with PUD who took no medication for it during pregnancy [56]. Meanwhile, no significant outcome difference was observed for those taking medication during pregnancy. The trend toward slightly increased though the insignificant risk of low birth weight and preterm birth might reflect more severe PUD symptoms among women taking PUD medication. PUD with endoscopic-

based diagnosis and PUD-related drug treatments do not increase the risk for congenital anomalies [45].

### 22.1.1.8 Specific Conditions

#### Zollinger–Ellison Syndrome

Zollinger–Ellison syndrome (ZES), described in 1955, is a PUD of the upper gastrointestinal tract that includes high levels of gastrin and gastric acid. There is little information on the management of pregnancy in patients with pancreatic endocrine tumors such as ZES. This has occurred because the syndromes are uncommon (i.e., 10/million population/year). Until the last decades, these patients frequently died soon after the diagnosis, which was often established only late in the disease course. The hormonal syndrome often causes severe metabolic or nutritional deficiencies that may interfere with pregnancy. However, because of earlier diagnosis and the increased ability to medically control the hormonal symptoms, especially in patients with ZES with potent gastric acid antisecretory drugs, these patients live longer, and women with the disorder more frequently become pregnant. The tendency of the tumor to grow slowly enables the physician to focus on symptomatic treatment. Gastrin levels do not change significantly during pregnancy [57] and thus are helpful for the diagnosis and follow-up of this syndrome. There is a controversy about whether pregnancy offers protection against ZES. Some have reported the absence of symptoms of ZES during pregnancy [58, 59], while others reported cases of exacerbation during pregnancy that required IV omeprazole treatment or even operation [60, 61].

The management of pregnant patients with asymptomatic pancreatic endocrine tumor syndrome, such as ZES, presents several unique problems. ZES is the most common symptomatic malignant pancreatic endocrine tumor. Like the other pancreatic endocrine tumors, these patients have two different treatment issues. First, symptoms caused by ectopic hormonal release must be controlled. Second, treatment must be directed against the tumor, which in all the syndromes, except insulinoma, is malignant in 30–90% of

cases, and 34% of patients have liver metastases; however, in most patients, the tumor grows relatively slowly [62]. Because of the slow rate of progression of most gastrinomas, the primary issue during pregnancy in patients with ZES is controlling the severe gastric acid secretion. This problem is complicated by the large volume of gastric acid secretion, necessitating high doses of gastric acid suppression. Also, high-dose safety profiles of gastric antisecretory drugs during pregnancy are unknown. If the ZES is diagnosed before pregnancy, curative resection with parietal cell vagotomy may obviate the need for gastric antisecretory drugs. If metastases are present or the diagnosis of ZES is made after conception, ranitidine, in the lowest possible dose, should be used to control acid secretion. If acid secretion is uncontrolled, the dose may be increased, or omeprazole may be used [63].

Antacids are generally ineffective in managing ZES and, thus, are not a realistic option.

The histamine H<sub>2</sub> receptor antagonists and H<sup>+</sup> -K<sup>+</sup> adenosine triphosphatase inhibitors can control gastric hypersecretion in patients with ZES (see Sect. 22.1.2.5). However, high doses are frequently required. The high doses used in ZES cimetidine can cause antiandrogen side effects [64]. Ranitidine, however, has not been shown to possess these antiandrogenic effects even at high doses [65]. There are case reports describing the safe use of cimetidine and ranitidine in pregnant patients with ZES [66]. A detailed strategy for treating patients with ZES before and during pregnancy is described by Stewart et al. [63].

#### *Helicobacter pylori*

*H. pylori* infection and NSAID use account for most cases of PUD. The rate of *H. pylori* infection for duodenal ulcers in the USA is less than 75% for patients who do not use NSAIDs. Excluding patients who used NSAIDs, 61% of duodenal ulcers and 63% of gastric ulcers were positive for *H. pylori*. These rates were lower in whites than in nonwhites. The prevalence of *H. pylori* infection in complicated ulcers (i.e., bleeding and perforation) is significantly lower than in uncomplicated PUD.

*H. pylori* infects the human stomach, causing gastritis, peptic ulcer, and gastric cancer. *H. pylori* infection has also been related to extra-gastric disorders. During pregnancy, preferential induction of Th2-type cytokines downregulates Th1-type responses, allowing fetal survival. The results suggest that *H. pylori* infection can activate resident uterine immune cells or recruit cells at the endometrial level. The local Th1-type response induced by *H. pylori* infection could alter the systemic Th1-/Th2-type cytokine balance at sites under particular physiopathological conditions of active tissue or vascular formation, such as pregnancy. This is the first evidence in an animal model of the possible influence of *H. pylori* infection on pregnancy. Transmission of *H. pylori* infection from the mother to the infant was not detected by culture in an animal study, suggesting that decreased baby weight may be due to decreased milk supply or altered nutrition from the mother [67]. Physiological and epidemiological evidence suggests that *H. pylori* may interfere with iron metabolism, lowering it [68]. The reduction in hemoglobin levels during pregnancy in the presence of *H. pylori* infection seemed to be slightly higher among women with iron therapy during pregnancy than women without [69]. Even though the difference between groups was not statistically significant, this pattern would be consistent with the hypothesis of a possible increase in bacterial density by iron therapy, which might, in turn, reduce the benefit of iron therapy because microbiologic and ferrokinetic studies suggested that outer membrane receptors of *H. pylori* in vitro can capture iron from human lactoferrin and use it for growth [70]. However, this hypothesis must be confirmed. Women who were infected with *H. pylori* were generally shorter than those who were not. Moreover, women who gave birth to babies with intrauterine growth retardation were shorter than those who gave birth to normal-sized babies. Many studies have shown that close contact and overcrowding among family members promote the transmission of *H. pylori* infection [71]. Therefore, the possibility exists that an infected mother may more often transmit *H.*

*pylori* to her infant and thereby continue a vicious growth restriction cycle.

The possible mechanisms by which *H. pylori* may affect fetal growth are speculative. However, it is conceivable that *H. pylori* infection is linked to increased dyspepsia, nausea, or vomiting [72] because of underlying undiagnosed PUD, which in turn may affect maternal appetite and restrict the growth of the fetus, although this was not determined. Another possible mechanism linking intrauterine growth retardation with *H. pylori* infection may be the effect of chronic *H. pylori* infection on the vascular system. Acute atherosclerotic changes have been noted in placental and uterine spiral arteries in cases with intrauterine growth retardation [73].

The *H. pylori* infection may increase platelet aggregation and fibrinogen and affect lipid peroxidase [74]. Therefore, chronic *H. pylori* infection might induce vascular disease, which may affect the placenta and cause intrauterine growth retardation. Therefore, a direct link between PUD and abnormal pregnancy or fetal consequences could not be proved because acute/chronic *H. pylori* infection and other potential confounders influence negative pregnancy outcomes. *H. pylori*-infected mice have decreased implantation rates, and their offsprings are of low birth weight [75]. Infection with *H. pylori* cytotoxin-associated gene (CagA)-positive strains has been shown to cause a severe inflammatory response and significant neutrophil infiltration in the gastric mucosa [76]. There is a statistically significant relationship between CagA-positive strains of *H. pylori* and early pregnancy loss (EPL), which might be explicable based on a general inflammatory reaction to infection.

Concentrations of IL-1 $\beta$ , IL-8, and TNF- $\alpha$  were all significantly higher in *H. pylori*-positive gastric mucosa [77]. These cytokines may cause systemic inflammation that could affect the integrity of the fetoplacental unit and threaten the welfare of the fetus (see Chap. 4).

### Gastric Outlet Obstruction

Several cases have been described [78, 79]. Ideally, the operation during pregnancy should be avoided due to surgical stress and possible

postoperative nutritional deficiencies to the mother and fetus. Gastric outlet obstruction should be treated with endoscopic balloon dilation with additional procedures such as endoscopic needle-knife radial incisions. The duration of the therapeutic effect depends on the underlying cause of gastric outlet obstruction. However, most studies report therapeutic effects in months, enough to postpone the definitive treatment by operation after delivery [80]. If malignancy is confirmed, surgery is indicated by oncologic principles in pregnancy (see Sect. 22.2.1).

### 22.1.2 Perforated Peptic Ulcer in Pregnancy

*I cannot remember a perforated gastric or duodenal ulcer during pregnancy.*

(Sir Gordon-Taylor)

*Every doctor, faced with a perforated duodenal ulcer of the stomach or intestine, must consider opening the abdomen, sewing up the hole, and averting a possible or actual inflammation by the careful cleansing of the abdominal cavity.*

(Johann von Mikulicz-Radecki, 1884)

#### 22.1.2.1 Historical Perspective

For thousands of years, healthy people have had acute abdominal pain, nausea, vomiting, and diarrhea, followed by death in a few hours or days. These symptoms often contribute to poisoning, and people have been sent to prison for this. King Charles I's daughter, Henriette Anne, died suddenly in 1670 (at age 26) after a day of abdominal pain and tenderness. Since poisoning was suspected, an autopsy revealed peritonitis and a small hole in the anterior wall of the stomach. However, the doctors had never heard of a PPU and attributed the hole in the stomach to the dissector's knife [81]. Necropsies were first allowed in 1500 and became more common between 1600 and 1800 [81]. Consequently, more often, perforation of the stomach was observed. Johann Mikulicz-

Radecki (1850–1905), often referred to as the first surgeon who closed a PPU by simple closure in 1884, said that “*Every doctor, faced with a perforated duodenal ulcer of the stomach or intestine, must consider opening the abdomen, sewing up the hole, and averting a possible or actual inflammation by careful cleansing of the abdominal cavity.*” Robert Daniel Mussey (Fig. 22.2) was one of the first, in 1927, who reported two cases of peptic ulceration in 370 operations during pregnancy at the Mayo Clinic in 10 years [82]. Whether these two operations were made in elective or emergent settings is unknown.

#### 22.1.2.2 General Population

The fluctuations in North–West Europe from 1790–1940 suggested three observable syndromes: gastric PPU in young women, duodenal PPU in young and middle-aged men, and gastric PPU in older men [84]. Perforations began to be



**Fig. 22.2** Robert Daniel Mussey (1884–1958) is a physician in a family of six generations of physicians (*cropped picture*) [83]. He guided the development of an obstetrics/gynecology department at the Mayo Clinic and was a Professor of Obstetrics and Gynecology there until he retired in 1950. (Reproduced with permission from [Flickr.com](https://www.flickr.com/photos/robertmussey/))

noted with increasing frequency at the beginning of the nineteenth century. Half of all perforations were then in young women in their twenties, which peaked in the latter half of the century. They seemed to be *acute gastric ulcers*, which caused death from perforations near the cardia or hemorrhage [84]. By the end of the century, this condition had begun to disappear. However, even in 1905, the Registrar General wrote: *Gastric ulcer does not frequently appear as a cause of death until the attainment of the reproductive period, when the female rate greatly exceeds the male, while at later ages, the male rate is in excess* [85]. The incidence of PPU during the 1940s in the two sexes was much greater in men, varying from 25:1 [86]. In the 1950s, however, there were signs that the volume of PUD had finally reached a peak and was beginning to fall. The lifetime prevalence of PPU has been estimated at 5% [87].

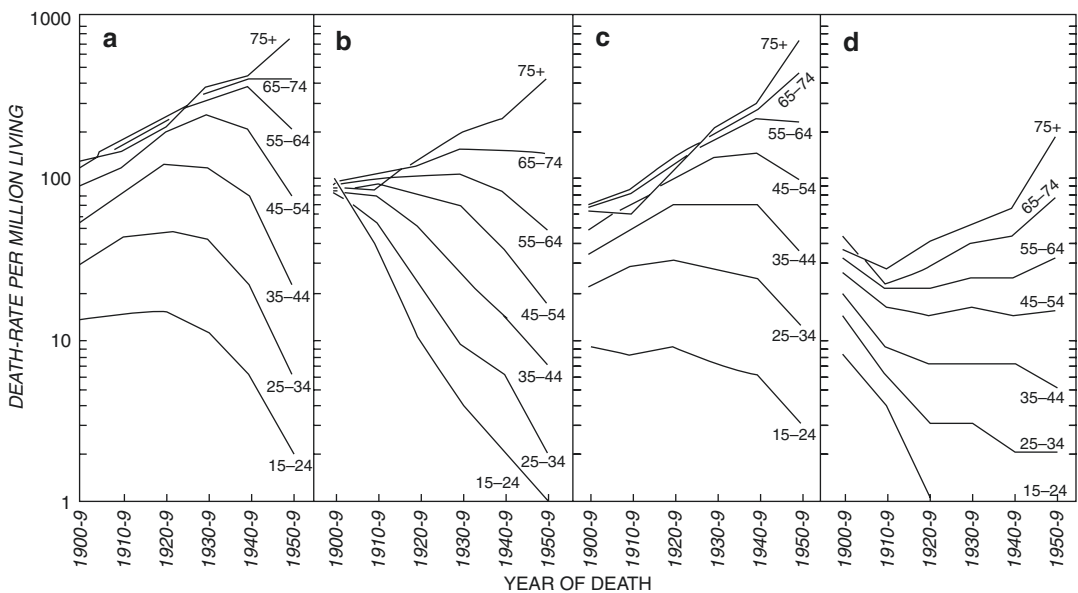
Trends for duodenal ulcers are similar but follow about 5 years behind. In the mid-1950s, death rates reached a plateau and began to fall [88]. Since the war, mortality from gastric and duodenal ulcers has declined in young men and

women, although until 1962, it was still rising at ages over 65 (Fig. 22.3). One possible explanation is that the fluctuations in PUD rates represent a *cohort phenomenon* and that each generation has carried its own particular risk of bearing ulcers throughout adult life. Because of the success of medical therapy in managing PUD, surgery has a limited role, and elective PUD surgery has been virtually abandoned. The number of elective operations for PUD dropped by >70% in the 1980s; 80% were emergent operations [89]. Currently, mortality and morbidity following PPU are substantial, with mortality rates as high as 25–30% [90]. The mortality incidence doubles for every 6-h period from the period of perforation to surgery. After 24 h, the mortality rate is maintained at a high rate of over 60%. Sepsis is frequent and a leading cause of death [91].

### 22.1.2.3 Pregnancy

#### Historical Perspective

In the pregnant population, Chabannes [44], in 1903, first drew attention to the subject, followed



**Fig. 22.3** Deaths from peptic ulcers by age and sex and year of death. (a) Gastric ulcer: males. (b) Gastric ulcer: females. (c) Duodenal ulcer: males. (d) Duodenal ulcer: females; mean rates for 10-year periods were calculated from the Annual Reviews of the Registrar General.

Populations include non-civilians. Correction factors for the pre-1940 data to allow for the change in death certification (males 1.034 and females 1.042) have not been used. Log graphs. (Reproduced with permission from [92])



by Szenes [93]. This point is further buttressed by the seminal work of Hooker in 1933, with only one case of the duodenal ulcer recorded following 1564 puerperal deaths from 348, 310 pregnancies [94]. Sandweiss et al. have subsequently reviewed the topic and found nine PPUs [4]. Howkins, in 1950, quoted Grey Turner's statement that *he has never seen undue activity of a peptic ulcer during pregnancy but is very familiar with the opposite state of affairs where ulcer symptoms disappear during pregnancy* and also Sir Gordon-Taylor's statement that *he cannot remember a perforated gastric or duodenal ulcer during pregnancy* [95] and it must be extremely rare to meet with this complication. William A. Scott, in 1945, discussing the differential diagnosis of acute abdominal conditions in pregnancy, does not even mention PPU [96], although there were already two case reports published by Anderson and Sandweiss et al. [15, 86].

### Incidence

in Detroit, during 1928–1937, the duodenal PPU was found in 1/70, 310 pregnancies and gastric PPU in 1/348, 310 pregnancies over 3 years in New York. Both patients died [4]. The low incidence of PUD in pregnancy has been demonstrated in several series from 1939 to 1955; PUD incidence was 11/233, 650 deliveries [6, 97, 98], and among 1564 maternal deaths in 348,310 pregnancies, only one death was due to PUD [99]. In early reports, PPU was more frequent than bleeding during pregnancy [4]. Up to 1971, there were 31 perforations (and 32 cases of hemorrhage) from PUD during pregnancy [3–5, 8, 18, 35, 39, 43, 86, 94, 100–132]. There are 40 cases published, half during pregnancy and another half during the early puerperium.

### Risk Factors

Risk factors for PPU are the same as for the PUD itself, such as fasting (Ramadan) [43] or adjustable gastric banding. The case does not define localization, macroscopic appearance, and whether the ulcer was peptic or related to silicone ring and local ischemia (*marginal ulcer*) [133]. Preeclampsia is a risk factor for bleeding PUD in pregnancy [134] and could also be a risk factor

for PPU. One-third of patients do not have risk factors.

### Ulcer Type

Most PPUs develop in the first part of the duodenum on the anterior wall in both pregnancy [3, 5, 18, 35, 39, 43, 102, 103, 107–117] and the puerperium [86, 94, 101, 118–132], a common location in the young nonpregnant population. Two cases (10%) of postpartum PPU were gastric [126, 131], but complete medical data were unavailable.

### Clinical Presentation

Clinical presentation is similar to the nonpregnant population: acute, severe abdominal pain, and vomiting are most common. Later pyrexia develops. Sandweiss et al. in 1943 stated that these signs during the second and third trimesters and the history of the preexisting ulcer should be considered warning signals of ulcer reactivation. Unfortunately, patients admitted to obstetric or gynecologic services are not questioned closely about past gastrointestinal symptoms, even if distress exists. The history of previous PUD attacks, although difficult to obtain, is the most important factor in diagnosing PUD [4].

It is difficult to notice abdominal distension in advanced pregnancy. Vital signs without evidence of bleeding should raise a suspicion of peritonitis and septic state—raised pulse, number of respirations per minute, and hypotension in the late phase [86].

The obstetric examination is initially normal and should raise suspicion of the nonobstetric cause of acute abdominal pain. Later in the course of undiagnosed peritonitis, spontaneous abortion or (preterm) labor can ensue.

### Puerperium

Some conclusions could be wrong because, in many cases, the pain started a day or two before the labor. At the same time, the diagnosis was established during the operation or after delivery, mostly during the first several days. Therefore, the duration of the disease until the diagnosis is mostly over 48 h [86, 94, 101, 118–132]. Anderson, in 1942, made one of the first classic

descriptions of puerperal duodenal PPU [86]. The extreme rarity of duodenal PPU [122] and diminished or subtle symptoms and signs in pregnancy and puerperium [101, 119] often cause a delay in diagnosis and surgical intervention. Nonspecific abdominal pain is experienced by 98 and 92% of primiparous and multiparous women, respectively [135]. After delivery, the relaxed and thin abdominal muscles may not respond actively with guarding or rigidity to underlying peritoneal inflammation [94]. Also, 60% of post-laparotomy patients will have evidence of pneumoperitoneum, which will take 1–24 days to be absorbed. This can be misleading as a normal finding. In suspected cases, water-soluble peroral contrast will show extralumination.

The obstetric examination is commonly normal [86] and should raise suspicion of the nonobstetric cause of acute abdominal pain. The PPU is equally frequent after cesarean section (CS) and vaginal delivery, although CS has dominated during the last several decades. After CS, these perforations occur during the first several days of puerperium. In the immediate postoperative period, abdominal symptoms may be interpreted as constitutional symptoms emanating from pregnancy or surgery [119]. Often a presumptive diagnosis of paralytic ileus is made and, in some instances, that of puerperal sepsis, which could result in a relaxed approach to dealing with such symptoms.

#### 22.1.2.4 Diagnosis

The only role radiology would have in the pregnant patient with PUD is confirmation of perforation. The usual approach in diagnosing pneumoperitoneum is plain abdominal X-rays [108]. The upright lateral chest radiograph confirms pneumoperitoneum in 98% of the cases. This is more sensitive than the upright posteroanterior chest radiograph, which shows the pneumoperitoneum in 80% [136]. The performance of a lateral chest radiograph excludes the fetus from the direct beam; if negative for the presence of free intraperitoneal air, this would support more conservative management. In the presence of strong clinical suspicion for intra-abdominal disease, the decision to perform further imaging,

such as abdominal CT, versus surgical exploration will have to be made on an individual basis.

#### 22.1.2.5 Treatment

The treatment of PPU consists of surgical intervention and perioperative pharmacological gastric acid suppression.

##### Surgical Treatment

In the first half of the twentieth century, there were cases of PPU in pregnancy treated conservatively. In 1943, Sandweiss et al. stated: “*When indications are present, pregnancy or puerperium should not be considered as a contraindication to surgical therapy*” [4]. Until 1966, 24 cases of PPUs have been described [4, 5, 8, 18, 35, 86, 101–107]. In that period, 16 patients (67%) were treated medically (nasogastric suction, nil by mouth, and antibiotics when available) with a maternal mortality of 100% and 11 infant deaths. James recorded the first successful suture closure of a duodenal PPU [18]. Omental patch repair with *H. pylori* eradication is the standard of care for duodenal PPU. The most common procedures in pregnancy and puerperium are the omental patch and suturing perforation. Postoperative complications such as intra-abdominal abscess [132] should be drained as soon as possible. If the adjustable gastric band is the cause of the marginal or peptic ulcer, it should be removed during an emergency operation [133]. Burkitt, in 1961, described the first emergency partial gastrectomy for a large duodenal PPU at the 31st week of gestation [102].

##### Perioperative Gastric Acid Suppression

###### Histamine<sub>2</sub> Receptor Antagonists (H<sub>2</sub>RA)

The H<sub>2</sub>RAs are the most used and safest medications for pregnant women with heartburn not responding to lifestyle modification and nonabsorbable medication. All four drugs (cimetidine, ranitidine, famotidine, and nizatidine) are FDA category B.

*Cimetidine and ranitidine.* Cimetidine and ranitidine have had considerable use in pregnancy over the last 30 years with an excellent safety profile. Only ranitidine’s efficacy has been

specifically studied during pregnancy for heartburn [137]. No adverse pregnancy outcomes or drug reactions were noted. Cimetidine has a weak antiandrogenic effect in animals [138], while ranitidine has no antiandrogenic activity in animals [65]. Neither H<sub>2</sub>RA has reports of human sexual defects in infants. The safety of cimetidine and ranitidine has been assessed in over 2000 pregnancies in database studies not sponsored by the manufacturers. In the surveillance study of 229,101 pregnancies in the Michigan Medicaid recipients between 1985 and 1992, a similar rate of major birth defects was detected (4.3% with cimetidine, 4.5% with ranitidine, and 4.3% in women taking no medications during their pregnancies) [139]. In summary, cimetidine and ranitidine have not been associated with an increased risk of congenital malformations [140–142]. Ranitidine is the only H<sub>2</sub>RA with documented efficacy in pregnancy.

*Famotidine and nizatidine.* There are much less reported safety data with these latter H<sub>2</sub>RAs than with cimetidine and ranitidine. Pregnant rabbits with the equivalent of 300 times the recommended human dose of nizatidine encountered abortions, low fetal weights, and fewer live fetuses [143]. On the contrary, rat studies found no adverse effects on fetal pups [144]. In the Michigan Medicaid Surveillance Study, 6.1% of fetuses exposed to famotidine during the first trimester of pregnancy developed major birth defects compared with the expected prevalence of one [139]. The small size was too small to draw firm conclusions, however. With nizatidine, there is only one case of a woman delivering a healthy baby after taking the drug during 14–16 weeks of gestation. Although few reports are available, famotidine appears safe during pregnancy. Although nizatidine was previously classified as FDA category C, the FDA recently reclassified it as a category B drug. However, the conflicting animal data are troublesome and suggest that other H<sub>2</sub>RAs may be safer during pregnancy. PPIs are the most effective drug therapy for symptom control and healing of esophagitis. The PPIs have not been as extensively used in pregnancy as the H<sub>2</sub>RAs, so the data about their efficacy or safety are less proven in pregnancy.

#### Proton-Pump Inhibitors (PPIs)

*Omeprazole.* The first of the PPIs is classified as an FDA category C because, at doses similar to those used in humans, omeprazole produced dose-related embryonic and fetal mortality in pregnant rats and rabbits [145]. No teratogenicity was observed. The FDA has received reports of at least 12 birth defects in pregnant women exposed to omeprazole, including anencephaly and hydranencephaly [139]. However, other case reports and small case series have found no infant congenital malformations in mothers taking 20–60 mg omeprazole/day, even in the first trimester of pregnancy [146]. A meta-analysis showed the relative risk for all major malformations among any PPI exposure of 1.18, a nonsignificant relative risk [147]. For the four studies where data for only omeprazole could be extracted, the relative risk was 1.05, also indicating a nonsignificant relative risk of malformations. Although the evidence suggests omeprazole is safe in pregnancy, the FDA has not changed its category C rating.

*Lansoprazole.* Animal studies using doses of lansoprazole up to 40 times the recommended human dose have found no evidence of impaired fertility or fetal toxicity. Human data on the safety of lansoprazole in pregnancy are more limited. In one nonobservational cohort study [146], six pregnant patients taking lansoprazole during the first trimester delivered seven healthy newborns. Lansoprazole was the only acid-suppressing with reported exposure in 13 infants from the Swedish Medical Birth Registry [142]. Two birth defects were observed: one atrial septal defect and one undescended testis. In a Danish study from 1999, 38 patients had taken PPIs during the first trimester of pregnancy (35 omeprazole and three lansoprazole) [148]. The prevalence of major birth defects, low birth weight, and prematurity was no different than in pregnant controls not receiving any medications. In another study, the rate of congenital abnormalities did not differ between the exposed and control groups: omeprazole 3.6%, lansoprazole 3.9%, and pantoprazole 2.1% versus controls 3.8%. No differences were found when exposure was limited to the first trimester [149]. The lack of teratogenicity in ani-

mals is reassuring, accounting for the FDA category C for lansoprazole use during pregnancy. However, the data on safety in human pregnancies are limited, and avoiding this and all PPIs, especially during the first trimester, are the safest course. If lansoprazole is required or inadvertent exposure occurs early in gestation, the fetal risk seems low. Based on product information from the individual manufacturers, the newer PPIs (rabeprazole, pantoprazole, and esomeprazole) have been shown safe in various animal studies. No reports describing the use of these newer PPIs during human pregnancies are available [139]. PPIs should only be used during pregnancy in women with well-defined complicated GERD, not responding to lifestyle changes, antacids, and H<sub>2</sub>RAs.

### Gastric Acid Suppression During Lactation

All systemic antireflux medications are excreted in breast milk and could harm the infant. Therapeutic options must be explained and discussed with women who require treatment but want to breastfeed. Drug safety during lactation has been assessed in animal studies and human case reports (Table 22.2).

#### Antacids

Aluminum and magnesium hydroxide antacids are not concentrated in breast milk and, thus, are safe during lactation. Neither Gaviscon nor sucralfate has been studied during lactation but is presumed safe because of limited maternal absorption.

#### Histamine<sub>2</sub> Receptor Antagonists

All H<sub>2</sub>RAs are excreted in human breast milk. Cimetidine and ranitidine reach concentrations in

breast milk 4–7 times the doses present in maternal serum [150]. In contrast, famotidine only reaches a mean milk-to-plasma concentration of 1.78, 6 h after ingestion [151]. Small amounts of nizatidine are excreted into human breast milk [152]. In the animal studies assessing H<sub>2</sub>RA safety during lactation, pups reared by lactating rats ingesting nizatidine experienced growth retardation [153]. The effects of H<sub>2</sub>RAs in breast milk on the nursing human infant are unknown. In 1994, the *American Academy of Pediatrics* classified cimetidine as compatible with breastfeeding [154]. Others also suggest that ranitidine and famotidine are safe, and the latter H<sub>2</sub>RA may be preferred because of the lower concentration in human breast milk. Nizatidine should be avoided in the breastfeeding mother because of the single animal study [153].

#### Proton-Pump Inhibitors

Little is known about PPI excretion in breast milk or infant safety in lactating women. PPIs probably are excreted in human milk because of their relatively low molecular weight. This was confirmed in the only report on PPI use during breastfeeding [155]. During the day, the patient fed her infant son just before taking omeprazole at 8:00 am, refraining from nursing for 4 h, and then expressed and discarded her breast milk at noon. At 3 weeks postpartum, blood and milk samples were obtained at 8:00 am and then every 30 min for 4 h. Breast milk levels of omeprazole began to rise at 9:30 am and peaked at 11:00 am at 58 mm, a considerably lower value than a simultaneous maternal level of 950 mm. The infant was doing well at 1 year. However, rats administered with omeprazole at 35–345 times

**Table 22.2** Safety of antiulcer/GERD medications during breastfeeding

| Medications | Safety | Comments                                                                |
|-------------|--------|-------------------------------------------------------------------------|
| Antacids    | Yes    | Not concentrated in breast milk                                         |
| Sucralfate  | Yes    | Minimal, if any, excretion in breast milk                               |
| Cimetidine  | Yes    | Compatible with breastfeeding ( <i>American Academy of Pediatrics</i> ) |
| Ranitidine  | Yes    | Excreted in breast milk in concentrations similar to cimetidine         |
| Famotidine  | Yes    | Lowest concentrations in the breast milk of all H <sub>2</sub> RAs      |
| Nizatidine  | No     | Growth depression in pups of lactating rats                             |
| PPIs        | No     | Growth depression in pups of lactating rats                             |

GERD gastroesophageal reflux disease, H<sub>2</sub>RA histamine<sub>2</sub> receptor antagonist, PPI proton-pump inhibitor

and rabeprazole at 195 times the recommended human dose during late pregnancy and lactation had decreased body weight gain of their pups [145]. Therefore, PPIs are not recommended for use by lactating mothers. Women can take PPIs, discontinue nursing, or use medications (i.e., H<sub>2</sub>RA) from another class.

### 22.1.2.6 Prognosis

The fetal outcome depends on two conditions in pregnancy. The first predictor of fetal outcome relates to long-standing PUD with its treatment during pregnancy (see Sect. 22.1.2.5). The second predictor is peritonitis from PPU. Delayed diagnosis has devastating consequences. In the 24 cases described up to 1966, 16 patients were treated medically with maternal and fetal mortality of 100% and 69%, respectively. Surgically treated patients had maternal survival of 100% with fetal mortality of 29% [4, 5, 8, 18, 35, 86, 101–107]. It is questionable how Paul et al., in 1976, found only six cases of maternal survival following PPU. Of these, only four were associated with the survival of the mother (maternal mortality 33%) and infant [114, 115]. Early surgical diagnosis and treatment followed by vaginal delivery at term offer the best chance for survival of the mother and child.

Maternal survival during pregnancy (without puerperium) approaches 100%, while fetal survival does not depend on the duration of PPU [3, 5, 18, 35, 39, 43, 102, 103, 107–117]. The maternal outcome from PPU in puerperium [86, 94, 101, 118–132] is similar to the PPU during pregnancy.

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## 22.2 Perforated Gastric Carcinoma

Perforated gastric carcinoma or malignant ulcer is an extremely rare condition due to the rarity of gastric cancer in the pregnant population. The characteristics of gastric cancer in young (pregnant) women are discussed for easier understanding and diagnosing such conditions during pregnancy.

### 22.2.1 Gastric Cancer in Pregnancy

#### 22.2.1.1 Incidence

Only 0.4–0.5% of gastric cancers occur in women aged less than 30 years [156]. The incidence of gastric cancer associated with pregnancy is comparatively low, found in 0.026–0.1% of all pregnancies [157, 158]. Fujimura and Fukunda first reported it in 1916 [159]. From 1969 to 1999, 31 cases of pregnancy-associated gastric cancer were published [160], with subsequent sporadic reports. On the other hand, partly due to Japan's relatively high incidence of gastric cancer, more than 100 cases were reported until 1987 [157]. The largest Japanese study had 137 patients adding to Ueo et al. [157] another 37 cases of pregnancy-associated gastric cancer from 1988 to 2007. These consisted of two cases in 1968–1977, six cases in 1978–1987, and 29 cases in 1987–2007 [161–163].

#### Krukenberg Tumor

The association between Krukenberg tumors and pregnancy is extremely rare. For over a century and its first description in 1896 by Krukenberg [164], there are 50 cases documented during pregnancy until 2016 [165]. The reported incidence of Krukenberg tumors with a primary gastric carcinoma in pregnancy is 2.6% [166]. The rarity of this stage is due to the rarity of gastric cancer in young women. Future incidence cannot be estimated. On the one hand, increasing incidence could be expected with increasing child-bearing of women over 30 years. Still, on the other, the incidence of (advanced) gastric cancer is declining in Western countries.

#### 22.2.1.2 Pathology

Gastric cancer in young adults shows female dominance with a male-to-female ratio of 1:1.5 [167], more aggressive histological features, an advanced disease stage at presentation, and a poorer prognosis [168]. These characteristics were even more pronounced in pregnancy-associated cases [158, 169]. While in older patients, most carcinomas are of the intestinal, usually well-differentiated type, the tumors in young patients are mainly poorly differentiated carcino-



mas of the diffuse type with signet ring cells and peritoneal metastasis. In Japan, the diffuse type is more common (86.9%) than the intestinal type (13.1%) in pregnant patients [161]. Also, in pregnancy, there is an increased rate of poorly differentiated tumors and signet cells [170, 171].

### 22.2.1.3 Pathophysiology

It has been postulated that immunosuppression during pregnancy is conducive to tumor growth. The biological and hormonal circumstances further enhance tumor progression [169, 172]. A suppressive effect of sex hormones on the spread of stomach cancer in the rat model was demonstrated [172]. The *H. pylori* infection rate is significantly higher in pregnant women than in nonpregnant women (26.6% vs. 11%) [173]. Furthermore, the secretion of gastric acid decreases during pregnancy, while the production of gastric mucus increases. Histaminase produced by the placenta deactivates histamine function; therefore, the patient exhibits no deterioration of symptoms caused by a malignant ulcer [174].

### 22.2.1.4 Clinical Presentation

#### Perforated Malignant Ulcer/Cancer

The presentation is the same as for PPU (see Sect. 22.1.2.3).

#### Krukenberg Tumor

Maternal and fetal virilization can be observed [175]. This virilization, nonspecific to Krukenberg, is due to luteinized ovarian stroma reaction stimulated by the placental production of steroids and human chorionic gonadotropin. The pelvic mass was found in 49.3% [166]. Its management during pregnancy is difficult. Indeed, the incidence of malignant tumors is only about 1–6% of adnexal masses associated with pregnancy. The differential diagnosis with luteomas or other benign adnexal pathology, where the management is radically different, is not always easy.

#### Gastric Cancer

Gastric cancer during pregnancy commonly presents in the advanced stage. Therefore, these patients present with abdominal pain, abdominal

distension, sometimes with a palpable abdominal mass, fullness sensation accompanied by early satiety, and nausea, sometimes vomiting [176, 177]. Sometimes the symptoms are mingled and masked by the hyperemesis gravidarum. Abdominal distension is difficult to estimate, especially in the second half of pregnancy, due to the associated physiologic abdominal distension during pregnancy. Weight loss is not pronounced because pregnant patients normally gain weight. The alarming symptom is too small weight gain during pregnancy with a normally developing fetus. Sometimes with abdominal symptoms, in the second half of pregnancy, uterine contractions or signs of preterm labor can be present [176]. Sometimes, symptoms are attributed to the pregnancy and not evaluated further until delivery or complications develop [158, 169].

### 22.2.1.5 Diagnosis

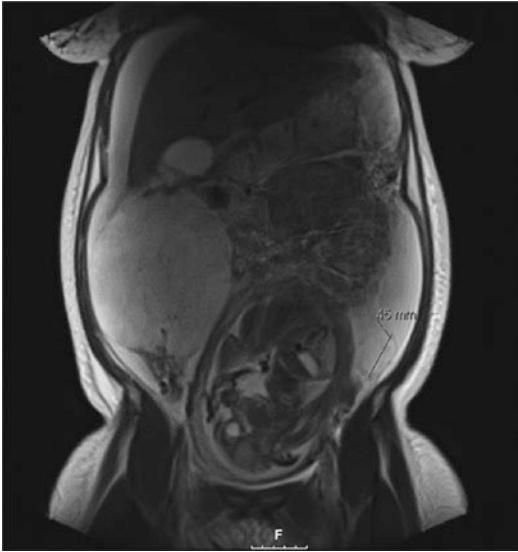
Laboratory findings commonly show anemia with elevated CRP [176].

As in nonpregnant patients, the diagnostic modality for definitive diagnosis is esophagogastroduodenoscopy (EGD). Indications for repeated EGD are the same as in nonpregnant patients. The lower threshold for the EGD should be the history of PUD [178].

In pregnant patients, MRI is preferred to a CT scan due to the ionizing radiation. Although not specific, the presence of solid components showing hypo-intensity on T2-weighted images in an ovarian mass appears to be a characteristic finding of Krukenberg tumors (Fig. 22.4), especially if the tumors are bilateral, have a sharp margin, are thin-walled, and have an oval configuration [179, 180]. Except for the primary tumor, the metastatic form can be found. Sometimes, the Krukenberg tumor misleads the clinician into diagnosing the primary ovarian tumor during pregnancy. Therefore, the definitive diagnosis is histological, marked by areas of mucoid degeneration and by the presence of signet ring cells.

### 22.2.1.6 Treatment

Patients with proven gastric cancer amenable to surgery are divided into four groups according to gestational age [157, 181]:



**Fig. 22.4** Coronal T2-weighted MR image shows a 29 weeks gravid uterus with well-defined bilateral oval ovarian masses (Krukenberg tumors) and extensive free fluid in the abdomen and pelvis. (Reproduced with permission from [179] under the CC BY 3.0)

*Group 1:* Gestational age <24 weeks. Surgery is indicated regardless of the condition of pregnancy.

*Group 2:* Gestational age 25–29 weeks. Surgery is indicated in the event of an advanced stage but resectable disease. However, surgery can be postponed in early-stage tumors until week 30 to ensure fetal viability and improve the perinatal outcome.

*Group 3:* Gestational age >30 weeks. Pregnancy should be ended via the vaginal route or CS, followed by surgery.

*Group 4:* Postpartum. Management is similar to that indicated in the general population.

In the event of complications (bleeding, perforation, peritonitis, etc.), surgery should be performed regardless of the condition of pregnancy or the gestational age.

The administration of chemotherapy (whether adjuvant or palliative) is possible after the first 3 months of pregnancy. In this regard, no data suggest an increased risk of fetal loss or anomalies, though an increased incidence of prematurity and

intrauterine growth retardation has been described [181]. The main chemotherapeutic agents are 5-FU, anthracyclines, and platinum drugs [181].

### Primary Gastric Tumor

A malignant ulcer is treated as a PPU initially (see Sect. 22.1.2.5). Subtotal or total gastrectomy in pregnancy is mostly done by an open approach. Laparoscopic gastrectomy in pregnancy can be performed [182], but it is not recommended due to the long operative time, increasing the rate of obstetric complications.

### Krukenberg Tumor

Aggressive surgery can improve the prognosis, but its management depends on the laparotomy findings and the duration of pregnancy. If no other metastatic disease except a bilateral Krukenberg tumor is found (Fig. 22.5), bilateral oophorectomy with or without hysterectomy is performed. The decision on the termination of pregnancy depends on the trimester of pregnancy and the patient's decision about the current pregnancy. The definitive procedure can be done in the same act as the known preoperative diagnosis is primary gastric carcinoma. Immunohistochemistry directs clinicians to primary tumors of gastrointestinal origin if the primary tumor is unknown. Then endoscopy reveals



**Fig. 22.5** Bilateral Krukenberg tumor at term pregnancy. (Reproduced with permission from [184] under the CC Attribution License)

the location of the primary tumor, and the final operation is performed according to the stage of the primary gastric carcinoma [183].

### Hormonal Therapy

The effect of estrogen and the results of antiestrogen treatment in clinical trials are controversial. The largest non-Japanese review reported that the features and prognosis of gastric cancer associated with pregnancy were the same as in non-pregnant young patients [160].

#### 22.2.1.7 Prognosis

##### Maternal Outcome

Almost all cases (96.7%) were advanced, and resectability was 47.5%. The patients who received gastrectomy had a high incidence of hospital death (22.7%) and a poor prognosis—21.1% 3-year survival [157] or maternal survival of 9–19 months after the diagnosis [170]. Most patients have poorly differentiated tumors with signet cells, which carry a poor prognosis [170]. Krukenberg tumors with a primary in the stomach carry a more daunting prognosis in pregnancy due to estrogen receptors in a high proportion of gastric carcinoma leading to aggressive behavior [185]. Therefore, the prognosis is extremely poor, i.e., 1-year survival of 14.5–18% and 2-year survival of 10.6–15% [157, 161, 165, 186]. Even regarding the 27 patients diagnosed in the most recent 20 years, the 1- and 2-year survival rates were 37 and 32%, respectively [161]. In conclusion, the prognosis of patients with pregnancy-associated gastric cancer remains poor, although it seems to be somewhat improved compared to the previous report [157].

##### Fetal Outcome

The estimated fetal survival rate is 70% and improves with advancing gestational age, with rates close to 100% in fetuses beyond 30 gestational weeks [165]. Increased rate of fetal distress, premature delivery, and fetal loss is observed with Krukenberg tumors from primary gastric cancer [179, 186, 187]. Although the placenta can be affected by metastatic disease [188],

no evidence suggests the tumor spread directly to the fetus [181].

### 22.2.2 Perforated Gastric Cancer in Pregnancy

#### 22.2.2.1 Incidence

Four cases of perforated gastric cancer during pregnancy exist: one from Turkey [189] and three from Japan [190–192]. There is one case of perforation of a carcinomatous stomach ulcer on the eighth day of puerperium [193].

#### 22.2.2.2 Treatment

For perforated gastric cancer, despite the stage of pregnancy, gastrectomy is the only possibility because simple sutures do not hold tissues together within the tumor mass. It is a palliative resection because the peritoneal cavity is already contaminated by cancer cells. Further therapy depends on the stage of pregnancy, as in other malignant tumors during pregnancy (see Sect. 22.1.2.6).

#### 22.2.2.3 Prognosis

One patient died 6 months after the initial diagnosis of gastric cancer despite surgical therapy and adjuvant chemotherapy [189]. Unfortunately, the data for three Japanese cases [190–192] and a perforated malignant ulcer [179] were unavailable.

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## 22.3 Spontaneous Gastric Rupture

### 22.3.1 Historical Perspective and Incidence

*Spontaneous gastric rupture* in the general population was the subject of medical speculation from 1819, but Carson's report in 1846 offered the first proof of its occurrence in humans [194]. Glassman, in 1929, collected 14 cases of non-traumatic rupture of the stomach from the literature [195]. Miller first reported spontaneous gastric rupture during labor or postpartum [196].

It is extremely rare, with a dozen published cases [196–206]. Detailed analysis reveals underlying pathophysiologic mechanisms (mostly associated with a diaphragmatic hernia) leading to gastric rupture. Therefore, it is questionable to diagnose spontaneous gastric rupture with these risk factors when the stomach is not in a normal intra-abdominal position.

## 22.3.2 Etiopathogenesis

### 22.3.2.1 Spontaneous Gastric Rupture

Spontaneous gastric rupture is rare because the stomach is anatomically protected in the upper abdomen by the liver and ribs and because the stomach has mobile distensible walls and two valves, gastroesophageal and pyloric, to decrease intragastric pressure.

It is apparent that the distention of the viscera invariably precedes rupture. Acute gastric dilation is a recognized complication of the postpartum period, primarily functional. Pylorospasm, “dropping” of the stomach and intestines to their antepartum position, hypotonicity of the bowel, and “nutritional edema” of the pylorus have been suggested factors in acute postpartum gastric dilation. Gastric rupture may be associated with additional factors, such as overdistension due to excessive fluid intake, oxygen therapy with nasal cannulae, or obstruction of the pyloric area by neoplastic processes or stenosis.

Most cases of *spontaneous* gastric ruptures in pregnancy are not truly spontaneous perforation and are associated with a diaphragmatic hernia [199–203, 205].

### 22.3.2.2 Intestinal or Gastric Obstruction

Gastric dilation and intestinal ileus are prone to occur after abdominal operations, especially when peritonitis is present. Whatever the cause of the dilation, sustained distention of the stomach may lead to ischemic necrosis of the mucosa with

disruption of this layer and subsequent extension through the remainder of the stomach wall [196, 207]. Nontraumatic rupture of the dilated stomach occurs most frequently near the lesser curvature. It explains this predilection by the external fixation of the lesser curvature and the reduced “elastic coefficient” of the “magenstrasse” [207, 208]. This lesser curvature predilection does not refer to gastric rupture of the intrathoracic stomach associated with diaphragmatic hernia or diaphragmatic rupture. In these situations, there is no predilection site [202].

The first factor leading to increased intragastric pressure is the dilation of its walls following the sudden consumption of large quantities of food. Historical studies on cadavers by Revilliod in 1885 indicate that the stomach has enormous capacity. Gastric rupture due to overfilling could occur only after a rapid filling of a stomach with 4 L of fluid. The rents occurred in the mid-stomach, both anterior and posterior walls [209]. Key Aberg, in 1897, did the experiment in a sitting position and found that filling with 4 L resulted in ruptures on the lesser curvature. Vomiting is a significant factor in Mallory–Weiss syndrome, causing longitudinal cracks in the gastric mucosa near the cardia. The cracks mentioned above may penetrate the muscular layer. Sometimes vomiting may lead to distal esophageal rupture (Boerhaave syndrome). The difference is that esophageal rupture occurs during vomiting with gastric contents, while gastric rupture occurs during nausea and vomiting reflexes. The pathogenesis of gastric rupture sometimes involves arterial ischemia of the gastric wall despite its excellent blood supply. Inflammation of the gastric mucosa is also a significant factor. Trauma, e.g., indirect cardiac massage or chest thump, is also causative [210]. The high position of the diaphragm intensifies the activity of the valve closing the gastric cardia. The stomach compression by the uterine fundus increases intragastric pressure and impairs gastric emptying. The probable inflammation of the gastric mucosa decreases the resistance of its walls. An enlarged gravid uterus can potentiate gastric migration into the thorax through a diaphragmatic hernia if present. Valsalva during the second stage of

labor may cause a rupture of an already distended stomach [199].

The pathologically dilated stomach becomes susceptible to rupture during forceful emesis when an abrupt increase in intra-abdominal pressure occurs [211]. Once the stomach becomes critically dilated, the lower esophageal sphincter functionally becomes a one-way valve, allowing contents only to enter the stomach. Such gastric ruptures typically occur on the lesser curvature where the stomach is less elastic. Important is the rapidity of onset and depth of the shock, and note that these patients die in the first 9–10 h without alleviating the state of shock by vigorous, supportive treatment.

Christoph and Pinkhamew, in 1961, believed that the pathogenesis of gastric rupture has a definite sequence in peritonitis [197]. The basis for acute gastric dilation was present because of the stress from perforation of the appendix and peritonitis, which may have spread following the involution of the uterus and spontaneous delivery. The distension was sufficient to cause ischemic necrosis of the gastric mucosa [196, 212] with a subsequent tearing of the outer layers of the stomach wall by the trauma of persistent emesis. Because of the surgical vent in the right lower quadrant, this case did not demonstrate the tympany and subcutaneous emphysema described by others [212]. Since postpartum gastric dilation and postoperative abdominal distention are frequent complications without causing “unexpected rupture” of a viscus, an additional factor must have had a vital role in the present case. Christoph and Pinkhamew, in 1961, believed that stress and chemical imbalance from her several difficulties may have produced changes in the gastric mucosa similar to those produced in major burns [197]. It seems probable that the subtly damaged gastric wall was thus more susceptible to ischemic necrosis and subsequent rupture than the normal stomach. Some authors believe that the term “spontaneous rupture” of the stomach is a misnomer and that “unexpected rupture” is a more descriptive phrase [197, 207]. In reviewing the available reports of the so-called spontaneous rupture of the stomach, a pathologic basis,

whether it was ulcer, carcinoma, or gastric dilation of undetermined cause, was demonstrated at operation or postmortem examination in all cases. Both cases of gastric rupture in pregnancy were on the greater curvature [196, 198].

### 22.3.2.3 Diaphragmatic Hernia

Gastric rupture can be due to incarceration and strangulation within a diaphragmatic hernia (see Chap. 6). With associated diaphragmatic hernia, it is difficult to claim the predilection location of the stomach rupture [196, 198, 205]. Another potential risk factor is preeclampsia [196, 213].

Most women are in the advanced third trimester of pregnancy or early puerperium, implying that the enlarging gravid uterus has a compressive role in gastric rupture [196–206].

### 22.3.2.4 Postbariatric Surgery

Gastric perforations occur after both restrictive and malabsorptive bariatric procedures. In restrictive, such as gastric banding, an inflating silicon band is placed around the stomach and reduces its orifice. The most common effect during pregnancy is repeated/intractable nausea and vomiting, resolved by deflating the silicon band. A *marginal ulcer* is a known complication of bariatric surgery. It results from tissue ischemia caused by the reduced blood supply to the stomach because of the inflated ring [214] or gastrojejunostomy after gastric bypass [215].

The general population has a high incidence of late postoperative complications after gastric banding. The rate of gastric band removal is 42–50%, with a median follow-up of 13–14 years [216, 217]. There are no cumulative data for the pregnant population, but due to the compression of the gravid enlarging uterus, the complications and potential removal rate could be higher.

## 22.3.3 Clinical Presentation

The patients commonly have initial symptoms such as nausea and vomiting. The characteristic finding of spontaneous gastric rupture is a symptomatic triad of [207, 208]:



- Tympanitic distention of the abdomen,
- Subcutaneous emphysema,
- Shock.

All three symptoms are not always present, especially in the early phase of this condition [196, 199]. Conditions increasing the risk of gastric perforation result in less dramatic clinical presentation. Obtaining a detailed medical history is important. Previous abdominal trauma can result in diaphragmatic tears leading the stomach to migrate into the thorax. Symptoms and signs include nausea, vomiting, and epigastric pain [196, 199, 203, 205], sometimes with referred pain in the left shoulder. Vomiting of dark-colored or even black contents, which do not look like enteric contents, should raise a suspicion that some underlying condition, such as ischemia or bleeding, is the cause of vomitus [196].

Reduced respiratory sounds are present on the affected side, commonly on the left [199, 203, 205] and commonly with chest pain and dyspnea [202, 203]. For the clinical presentation of intrathoracic perforation, see Sect. 20.3.3.

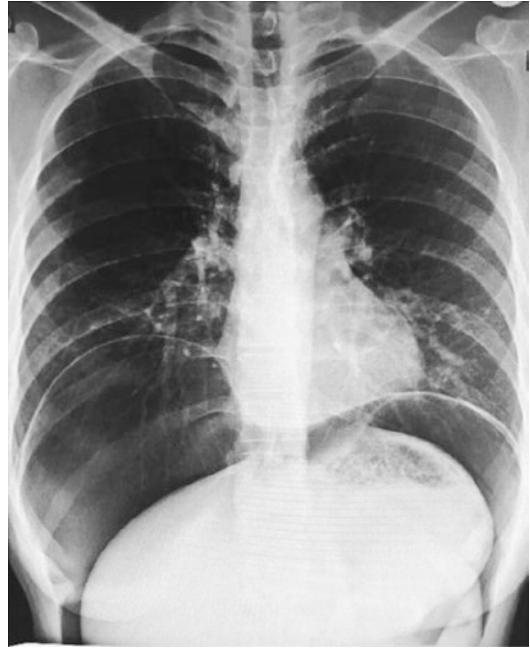
## 22.3.4 Diagnosis

### 22.3.4.1 Laboratory Findings

WBC and CRP are elevated. In advanced peritonitis, elevated BUN and creatinine result from the fluid shift in the third space.

### 22.3.4.2 Plain Abdominal or Chest X-Ray

With intra-abdominal position, gastric rupture presents with massive pneumoperitoneum on plain abdominal X-ray (Fig. 22.6). Chest X-rays reveal an infiltrate, mostly in the lower lobes, with a small pleural effusion [203]. The sudden development of severe dyspnea and chest pain should raise suspicion of hollow viscus perforation/rupture of the intrathoracic location of organs [201]. Also, when clinicians erroneously drain pleural effusions or pneumothorax fluid, a large quantity of coffee ground colored [201] or biliary fluid [205] should raise a suspicion of a stomach perforation/rupture in the thorax.



**Fig. 22.6** Chest X-ray shows massive free gas under both hemidiaphragms with notice of the gastric band. (Reproduced with permission from [218] under the CC Attribution License)

### 22.3.4.3 Esophagogastroduodenoscopy

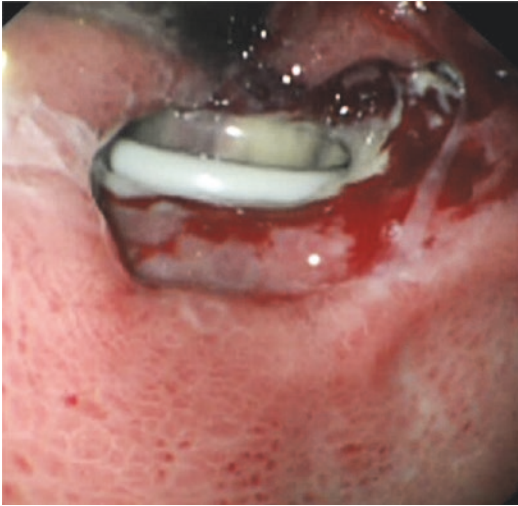
Erosion of the gastric band before the development of gastric perforation or in its early phase can be detected by esophagogastroduodenoscopy (Fig. 22.7).

### 22.3.4.4 Abdominal CT

An abdominal CT scan is used in doubtful cases. Pneumoperitoneum is easily detected [218], or peroral contrast is used to detect the location of extralumination.

## 22.3.5 Differential Diagnosis

With the sudden presentation of severe symptoms, the most common differential diagnoses are myocardial infarction, pulmonary embolism [205], or spontaneous pneumothorax. Different differential diagnoses include gastroenteritis [199, 201] and acute pancreatitis with an acute, less severe presentation with nausea and vomiting. Similar but less exaggerated symptoms are



**Fig. 22.7** Esophagogastroduodenoscopy shows a completely eroded band through the gastric wall, located almost intraluminal. Also, the scope could not pass beyond the band. (Reproduced with permission from [218] under the CC Attribution License)

present with hiatal or diaphragmatic hernia (see Sect. 20.3) or pneumonia with effusion [203]—the diagnoses that lead to delay of treatment.

## 22.3.6 Treatment

### 22.3.6.1 Surgical Treatment

In most cases, with simple rupture or perforation, debridement of the edges around the perforation and primary sutures in two layers suffices. If a larger part of the stomach is avital, resection with a form of gastropasty is performed [206]. When a diaphragmatic hernia or tear is present, concomitant diaphragmatic hernia repair should be made (see Sect. 20.6.2) [205]. With intrathoracic perforation, the insertion of a thoracic drain prevents empyema formation [205].

When the patient with a gastric band deteriorates under conservative management and a laparotomy is performed, the removal of the ring is necessary to resume appropriate gastric blood supply, which is important for proper gastric healing. Firm adhesions with surrounding tissues and organs can be present in chronic inflammation with erosion. Sometimes segmental gastrec-

tomies are completed with gastrogastrostomy [218].

### 22.3.6.2 Obstetric Management

Obstetric management depends on the status of the fetus at the presentation. If stomach rupture occurs intra-abdominally, preterm labor is common. If the treatment of gastric rupture is delayed, intrauterine fetal death or delivery of the stillborn can be expected. If fetal distress is present, surgical treatment of gastric rupture is accompanied by simultaneous CS. Pregnancy may continue if there is a question of fetal maturity without fetal distress. In cases when diaphragmatic hernia repair accompanies the treatment of gastric rupture, simultaneous CS minimizes the possibility of disruption of the diaphragmatic hernia suture line.

## 22.3.7 Prognosis

Early suspicion and diagnosis, early aggressive resuscitation, and emergency laparotomy are keys to maternal and fetal survival. Treatment delay >12 h can increase the odds of fatality [199, 204]. During the last 50 years, maternal and fetal survival has been nearly 100% [196–206]. High fetal survival should be interpreted cautiously because many women develop gastric rupture near term or during early puerperium when fetal mortality is significantly reduced.

Weiss et al. reviewed the results of seven pregnancies after gastric band placement, five of which had progressed to delivery [219]. All bands were decompressed because of nausea and vomiting without gastric perforation.

## 22.4 Intestinal Perforation

If intestinal obstruction with perforation and inflammatory bowel diseases are excluded (see Chaps. 18 and 21), small and large bowel perforation is extremely rare during pregnancy. The most common causes are intestinal endometriosis, colorectal carcinoma, instrumental abortion, and spontaneous or idiopathic perforation.

## 22.4.1 Intestinal Endometriosis

### 22.4.1.1 Introduction

Endometriosis is the presence of the endometrium outside the uterus and usually affects pelvic structures, including the bowel. Intestinal involvement occurs in 5–12% [220] of patients with endometriosis. The most frequent location is the sigmoid colon, followed by the rectum, ileum, appendix, and cecum [221]. The most accepted theory of endometriosis is the peritoneal implantation of the endometrium by retrograde menstruation or the possible metaplasia of peritoneal cells. Intestinal endometriosis may be found in every layer of the bowel wall. It is most common within the subserosa as superficial serosal implants [222, 223]. *Deep bowel endometriosis* is a solid mass deeper than 5 mm under the peritoneum [224]. Under cyclical hormonal influences, these implants may proliferate and infiltrate the intestinal wall and cause a fibrotic reaction with the formation of strictures and adhesions, which may lead to bowel obstruction and recurrent abdominal pain [225, 226]. On the other hand, transmural bowel wall involvement is not so common. The intestinal mucosa usually remains intact, and perforation of the affected intestinal tract is very rare [223, 227].

### 22.4.1.2 Incidence

Endometriosis causes lower fertility rates. Fortunately, assisted reproductive techniques give these patients good chances to become pregnant even if endometriosis is not completely removed. The result is a possible higher incidence of endometriosis-related complications during pregnancy. One of these is bowel perforation due to retained bowel endometriosis. The additional problem could be the influence of IVF on the endometriosis recurrence rate of 7% at 12–21 months after IVF [228, 229]. Other studies, fortunately, did not confirm these results, but this topic should be kept in mind [230, 231].

Until 2019, less than 40 of intestinal perforation (appendiceal perforation excluded, see Chap. 15) from endometriosis in the general population have been reported [232, 233] and >50% during pregnancy and puerperium. The first case in preg-

nancy, with the perforation located on the jejunum, was described by F. Haufler in 1931 [234].

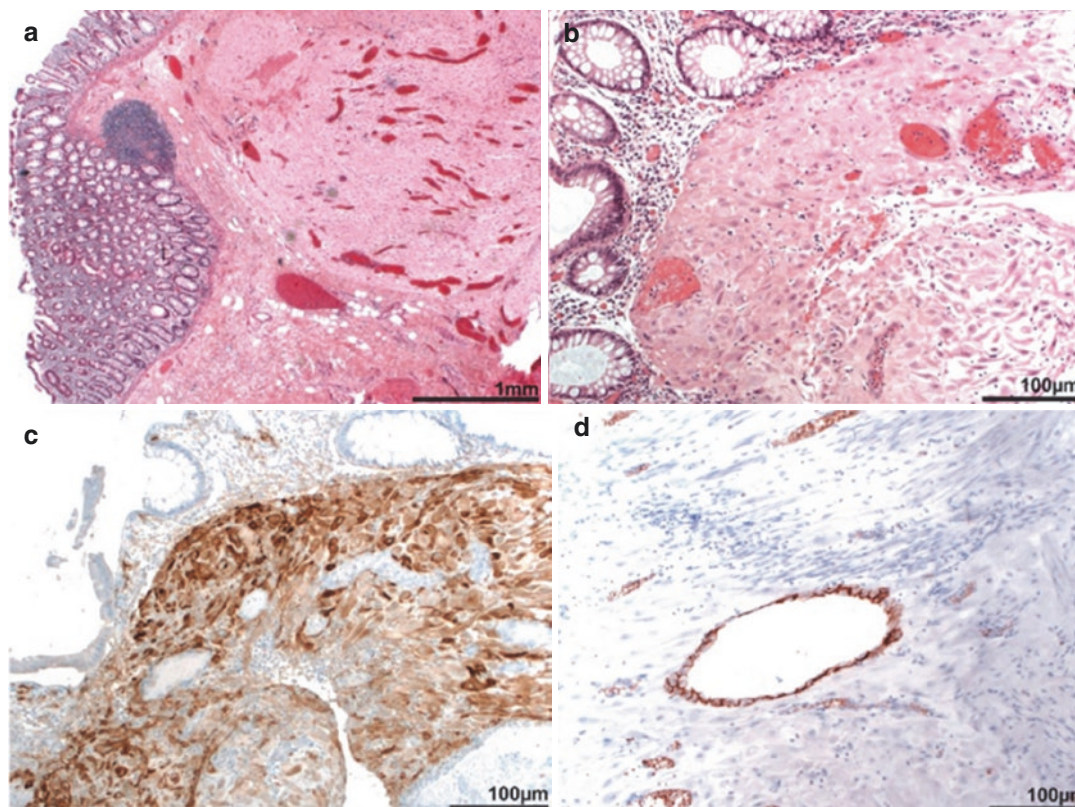
When appendix vermiformis is excluded (which presents as acute appendicitis), the rectosigmoid colon is the most common site of perforation from endometriosis in the pregnant population. It accounts for >60% of cases in pregnancy [213, 225, 234–247]. Almost all intestinal perforations occur in the third trimester or puerperium.

### 22.4.1.3 Pathophysiology

The preexisting endometriosis-derived ectopic decidua is very similar to de novo ectopic decidua. A history of endometriosis and the presence of glandular endometrial structures can aid in differentiation. De novo ectopic decidua is usually asymptomatic and found incidentally during CS, mostly on ovarian surfaces or the uterine serosa. Endometrial glands with decidualized stroma are observed in the submucosa, suggesting that the pathogenesis of ectopic decidua is preexisting endometriosis.

McArthur and Ulfelder observed that the area of the endometrium had become decidualized and enlarged during the first trimester and had undergone decidual necrosis with contraction during the third trimester. After pregnancy, there usually was a continued reduction in the size of the endometriotic lesions. This contraction in an area already weakened by endometrial stromal infiltration can cause perforation [222, 248]. In those patients with intestinal perforation, the entire intestinal wall is replaced by endometriotic tissue (Fig. 22.8). In pregnancy, under the effect of progesterone, the area of ectopic endometrium becomes decidualized with a progressive size reduction [248, 249]. The decrease in size of a transmural endometriotic nodule may lead to perforation, by weakening the intestinal wall [222], particularly in the third trimester, which is the time of perforation in most reported cases [222, 235, 248]. Moreover, decidualization causes a severe inflammatory response with an increased





**Fig. 22.8** Acute endometriosis-related sigmoid perforation in pregnancy. (a) Endometriosis with decidualized endometrioid stroma infiltrating large bowel wall, mucosa, and submucosa ( $\times 25$ ); (b) decidualized endometrioid stroma in mucosa and submucosa ( $\times 200$ ). (c)

Immunohistochemistry for CD10 demonstrating endometrioid stroma ( $\times 200$ ). (d) Immunohistochemistry for epithelial marker Ber-EP4 demonstrating sparse endometrioid glands in the endometriosis ( $\times 200$ ). (Reproduced with permission from [251] under the CC BY Attribution License)

number of natural killer cells and decidual changes, which are responsible for a higher risk of perforation [249, 250]. Additionally, perforation can also be facilitated by the progressive traction of the enlarged uterus on the strictly adherent surrounding bowel loops and, consequently, on the decidualized and weakened area of the bowel wall [235]. Moreover, constipation is common in pregnancy, so intestinal stenosis due to endometriosis may cause an increase in intra-intestinal pressure and subsequent intestinal perforation. Although endometriosis improves during pregnancy, the cases described show the potential occurrence of severe and unexpected complications of the disease. Besides endometriosis, colorectal stenosis can result from pre-pregnancy colorectal resection from deep pelvic endometriosis. Whether the residual colorectal endometriosis or stenosis is a

risk factor for colorectal perforation during pregnancy is unknown [238].

Symptomatic pre-pregnancy intestinal endometriosis should be treated surgically before pregnancy, minimizing the possibility of spontaneous intestinal perforation during late pregnancy [244]. Also, removing intestinal endometriosis results in significant pain relief and improved quality of life.

#### 22.4.1.4 Clinical Presentation

The symptoms and signs of the acute abdomen are present with intestinal perforation. Before perforation, abdominal pain could be cyclical, as in endo-

metriosis. Prepregnancy endometriosis is detected in 31% [252]. The location of the pain depends on the part of the intestine infiltrated with endometriotic nodule(s). Therefore, if appendix vermiformis is involved, acute appendicitis is a classic presentation (see Chap. 15). Sometimes, the duration of pain before the perforation can be several weeks [213]. Larger nodules infiltrating the intestinal muscular layer cause a wide range of symptoms, including dyschezia, constipation, diarrhea, abdominal bloating, painful bowel movements, the passage of mucus in the stools, and cyclical rectal bleeding [253, 254]. The symptoms associated with intestinal endometriosis often mimic diarrhea-predominant or constipation-predominant irritable bowel syndrome [255]. Enlargement of endometriotic nodules could aggravate constipation or initiate abdominal distension due to impaired bowel peristalsis. Also, due to transmural involvement, the patient can present with GI bleeding before or during perforation.

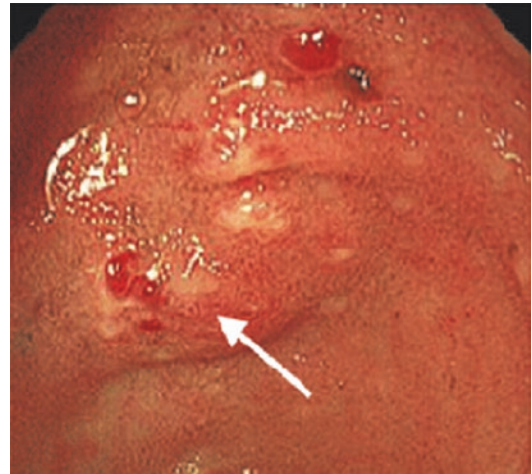
#### 22.4.1.5 Differential Diagnosis

The differential diagnosis may be particularly challenging before intestinal perforation due to a wide range of symptoms. The rareness of intestinal perforation and the symptoms suggestive of pyelonephritis or diverticulitis may mislead and delay the diagnosis, especially before the perforation ensues.

#### 22.4.1.6 Diagnosis

Standard laboratory investigations and plain abdominal X-rays are made with the suspected acute abdomen. Bowel perforation results in pneumoperitoneum. Before the presentation of the acute abdomen, the patient with abdominal pain can be investigated by colonoscopy. If endometriotic nodules are transmural, they can protrude through the intestinal mucosa with or without signs of (sub)mucosal bleeding (Fig. 22.9). It is difficult to diagnose rectal perforation when a patient presents with progressive nonspecific low abdominal pain. Sometimes laparoscopy is diagnostic [241].

Most current guidelines and recommendations do not mention the diagnostic algorithm for intestinal endometriosis during pregnancy [256–260].



**Fig. 22.9** Endoscopic image of the sigmoid colon with endometriotic infiltration of the bowel wall. Protruding spot with a small erosion (white arrow). (Reproduced with permission from [213])

#### 22.4.1.7 Treatment

Appropriately managing these patients may be challenging, and a multidisciplinary approach is mandatory for good outcomes. The best approach is *en bloc* resection of endometriosis and associated segment of a perforated bowel. With small bowel perforation, resection with anastomosis is recommended, or ileostomy for prolonged peritonitis. With sigmoid colon perforation, Hartmann's operation is the procedure of choice [241].

Most current guidelines and recommendations do not mention the management of intestinal endometriosis during pregnancy [256–260].

#### 22.4.1.8 Prognosis

Endometriosis was confirmed histologically in all the evaluated specimens. Decidualized endometriosis involving the entire intestinal wall was found in 88%. Fetal survival is 100%, with a mean gestational age near term [247, 252]. The common finding is several days between the onset of symptoms and fetal distress with emergency delivery [247]. Most newborns did not require any specific treatment. Alterations of the local endometrial environment in patients with endometriosis result in late-stage disturbances following an adverse ripple effect in the early stages [261]. Therefore, it is interesting that



intestinal perforation has excellent fetal outcomes with the opposite of the adverse impact of endometriosis on obstetric outcomes.

## 22.4.2 Bowel Perforation

### 22.4.2.1 Colorectal Carcinoma

See Sect. 18.6.

### 22.4.2.2 Stercoral Colorectal Perforation

#### Incidence

Stercoral perforation is rare, even in nonpregnant patients. The first case of (possible) stercoral perforation was described in 1894 by Pavy [262]. There were only 88 cases from 1894 to 2000. Stercoral perforation during pregnancy is extremely rare, with only four published cases in the second half of pregnancy [263–266].

#### Risk Factors

Chronic constipation is the main risk factor in 81%. The use of antacids, codeine-containing narcotics, nonsteroidal anti-inflammatory agents, major tranquilizers, and tricyclic antidepressants has been linked to stercoral perforation [267, 268]. These medications are all known to cause constipation.

#### Diagnosis

Proposed diagnostic criteria for stercoral perforation are [269]:

- Round or ovoid perforation,  $\geq 1$  cm in diameter, antimesenteric location,
- Fecaloma (hard, laminated, inspissated fecal mass) within the colon, protruding through the perforation site, or lying within the peritoneal cavity,
- Typical pathohistological features (pressure necrosis or ulcer with chronic inflammatory reaction around the perforation site),
- The absence of other active colonic pathologies, such as diverticulitis, carcinoma, and Hirschsprung's disease.

#### Treatment

Treatment is surgical, and resection of the diseased segment with proximal colostomy and closure of the rectal stump or mucous fistula are the procedures with the lowest mortality rate in the general population [267]. This is the recommended procedure in the pregnant population, performed in three cases [264–266].

#### Prognosis

The reported mortality rate among all cases in a general population of stercoral perforation is 47%, with a 35% mortality rate after surgical treatment [267]. Of four pregnant patients [263–266], one died (maternal mortality of 25%). Perinatal mortality is 50%, probably due to prolonged peritonitis.

### 22.4.2.3 Colorectal Obstruction and Pseudo-Obstruction

See Sects. 18.1.4.3 and 18.6.

### 22.4.2.4 Spontaneous Intestinal Perforation

#### Incidence

This is an extremely rare entity, and the incidence is unknown. In 1959, seven cases of nontraumatic/nonendometriotic intestinal rupture were reported during pregnancy, with 85% mortality [207].

#### Risk Factors

All risk factors for “spontaneous” ischemic events in the general population are also risk factors in pregnancy (Table 22.3). The difference is in the incidence of different risk factors due to the specific age of presentation. Also, pregnancy per se is a risk factor for thromboembolic events. The combination of different risk factors could be present and should be kept in mind, which aggravates the possibility of intestinal ischemia and subsequent perforation. Most spontaneous intestinal perforations are due to previously unknown but present risk factors. There are cases when women during early pregnancy (by mistake because they are unaware of pregnancy) [270] or early postpartum take oral contraceptives by themselves [271] with the development of mes-

**Table 22.3** Risk factors for spontaneous intestinal perforation [272–274]

|                                                   |
|---------------------------------------------------|
| Antiphospholipid syndrome (macroangiopathy)       |
| HELLP syndrome (microangiopathy)                  |
| Syphilis                                          |
| Vasculitis                                        |
| Low-flow states                                   |
| Arrhythmia                                        |
| Sepsis                                            |
| Shock                                             |
| Disseminated intravascular coagulation            |
| Recent surgery/C-section                          |
| Thromboembolism                                   |
| Ischemia caused by previous surgical manipulation |
| Cocaine abuse                                     |
| Valvular heart disease                            |
| Infective endocarditis                            |
| Diabetes mellitus                                 |
| End-stage renal disease                           |
| Idiopathic hypertension                           |
| Oral contraceptives                               |

enteric vein thrombosis. These risk factors are the same and could include small and large bowel perforation.

### Prevention

Obstetric complications are the other hallmark of antiphospholipid syndrome. It is recommended that women with antiphospholipid syndrome should maintain antithrombotic treatment throughout the entire pregnancy and postpartum period. The prevention of choice is combined low-dose aspirin and full antithrombotic doses of low molecular weight heparin. In high-risk groups, such as the history of previous thrombotic events, warfarin may be used during pregnancy but only after organogenesis (6th–12th weeks) because of the high risks of fetal malformations.

### Treatment

The type of operation depends on the extent of peritonitis and underlying ischemia. If the perforation is present without visible ischemia, resection with anastomosis is the preferred method. If there are signs of ischemia, the ischemic segment is resected, and anastomosis with or without stoma is performed. In long-standing generalized peritonitis, the stoma is the preferred option.

### 22.4.2.5 Transvaginal Instrumental Abortion

#### Incidence

See Sect. 18.3.2.

#### Risk Factors

See Sect. 18.3.3.

#### Clinical Presentation

Uterine perforation with bowel injury from instrumental abortion has three distinct clinical presentations. Small bowel obstruction due to incarceration through the uterine perforation and mesenteric injury resulting in bleeding is described in Sect. 18.3.5. The third presentation results from a bowel perforation. In all presentations, the clinical picture depends on the delay in the diagnosis. If bowel injury is suspected or proven during an instrumental abortion, immediate surgery is performed during the same anesthesia and without progression of bleeding, obstruction, or peritonitis. As many instrumental abortions are illegal and not performed in hospitals, many women present hours to days after the abortion. Many of these women refuse to confirm previous illegal abortions, which complicates establishing the correct diagnosis [275]. With bowel perforation, patients present with pelvic pain, spreading to the entire abdomen in advanced cases. Blood pressure is initially normal, with tachycardia, and with the progression of the spread of luminal contents, sepsis occurs, and patients become hypotensive. Fever over 38 °C develops early in this condition [276]. The abdomen is distended, and vomitus can be present [276]. During the examination, peritoneal irritation is present [277], with foul-smelling vaginal discharge [275] or even feces passing through the vagina [277]. Uterine injury results in vaginal bleeding [276].

#### Diagnosis

Serum C-reactive protein and leucocytes are elevated with neutrophilia and left shift.

Plain abdominal X-rays reveal free gas under the dome of the diaphragm indicating perforation of the hollow viscus. Paralytic ileus can be due to

peritonitis in the classic form of air–liquid levels.

If plain abdominal X-rays are inconclusive, transabdominal ultrasound is made. Further imaging diagnostic modalities include abdominal CT or MRI (see Sect. 18.3.4).

## Treatment

### Surgical Treatment

Surgical intervention is the standard treatment for bowel injury/perforation following instrumental abortion [278]. All patients underwent surgical treatment [276, 278–284]. One factor affecting the surgical outcome of bowel perforation is the interval from perforation to laparotomy [278]. Early surgery can minimize complications, while delayed surgery leads to severe peritonitis and septic shock. Most patients in developing countries were operated on more than 24 h after the onset of illness [276, 278]. Delayed definitive surgery may be attributed to late presentation due to a lack of accessibility to healthcare facilities and awareness of the disease. As a result, some patients with bowel perforation following induced abortion take medications in the prehospital period with the hope that the symptoms will abate [275]. It is also possible that some clinicians initially managing the patients may not have considered perforation as a possible diagnosis leading to delayed referral to tertiary care hospitals.

The surgical management of small intestinal injuries is straightforward, with a minimal sequel. If the patient undergoes exploration within 24 h of the small bowel injury, a simple closure of solitary perforations (after debridement of the devitalized edges of the perforation) or segmental intestinal resection and primary anastomosis in multiple perforations or gangrenous bowel is indicated. After 24 h from injury, ileostomy, with or without small bowel resection, is recommended [277]. The management of large bowel injuries is more controversial [278, 281]. This is more so when the left colon is involved. A simple colostomy has been reported to be the safest approach. Other options include primary repair, resection with primary anastomosis, or a repair

with a proximal protective colostomy or ileostomy. A simple colostomy is easier and faster to accomplish in these poor surgical-risk patients. However, the major drawback of colostomy is the need for a second operation to restore intestinal continuity, the specialized care before closure, and the attendant cost [276, 278–284]. The challenge is even more conspicuous in a developing country like Tanzania, where resources for stoma care are limited, and peristomal ulceration remains a major issue [276, 278–284].

### Obstetric Management

See Sect. 18.3.7.3.

### Prognosis

The recent overall complication rate in developing countries is up to 50% [276, 281]. The difference in complication rates can be explained by differences in antibiotic coverage, meticulous preoperative care, proper patient resuscitation before the operation, improved anesthesia, and a better hospital environment. Surgical site infection was the most common postoperative complication [281, 282]. The high surgical site infection rate may be attributed to the contamination of the laparotomy wound during the procedure [285]. Maternal mortality ranges from 8 to 27% [276, 281, 282, 285]. The high mortality rate is attributed to high gestational age at the termination of pregnancy, late presentation, delayed surgical treatment, and postoperative complications. Maternal survival depends on the type of operative procedure used for colonic injuries. When a defunctioning colostomy is performed, the mortality is nil. In patients with simple closure of the perforation and those with primary resection and anastomosis, mortality is 66.6% [286]. After removing the devitalized edges, primary closure of the colonic perforation is an option only when recognized during an instrumental abortion.

The median length of hospital stay is variable, from 12 days [281] to significantly longer hospitalizations [282]. Self-discharge against medical advice is a recognized problem, and this is rampant, especially among patients with complications of illegally induced abortions. Similarly, poor follow-up visits after hospital discharge

remain a concern. These issues are often the results of poverty, a long distance from the hospitals, and ignorance.

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## Abstract

There has been a dramatic increase in bariatric surgeries performed to manage morbid obesity, with Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy being the most frequent. Women comprise 80%, and 75% are 18–49 years old. Morbidly obese patients have lower fertility, and bariatric operations result in increased fertility rates and better fetal outcomes in patients with reduced excessive weight. As in the general population, intussusception and internal hernia are the most common complications. A plain abdominal X-ray is commonly normal and leads to a delay in diagnosis. Abdominal CT or MRI is diagnostic and should be done in patients with symptoms of intestinal obstruction after a pre-pregnancy bariatric operation. The treatment is surgical. In the early course of these conditions, laparoscopic desincarceration of internal hernia or desinvagination of intussusception is successful. In delayed diagnosis, open procedures are frequent and commonly result in intestinal resections due to bowel gangrene. An increased rate of acute cholecystitis is recognized after pre-pregnancy RYGB. Therefore, transabdominal ultrasound of the gallbladder is mandatory with acute right upper quadrant pain in these patients.

## 23.1 Bariatric Surgery and Pregnancy

### 23.1.1 Introduction

There has been a dramatic increase in bariatric surgeries performed to manage morbid obesity, with Roux-en-Y gastric bypass (RYGB) comprising the most frequent procedure performed in the USA [1, 2]. Women comprise 80%, and 75% are 18–49 years old [3]. Laparoscopic sleeve gastrectomy (LSG) is gaining popularity due to similar results and technically easier operation. Weight loss is likely to reduce infertility and increase sexual activity, increasing pregnancy rates.

*The American College of Obstetrics and Gynecology recommends losing weight before conception and acknowledges bariatric surgery as promising in pre-pregnancy obesity treatment [4].*

### 23.1.2 Complications

In the general population, small bowel obstruction occurs in 3.6–9.3% of patients after RYGB depending on the duration of follow-up [5, 6]. Internal hernia (IH) is the most common cause

(42–61%), followed by adhesions (22%), jejuno-jejunoscopy stenosis (15%), and incisional hernia (9.3%) [5, 6]. The incidence of small bowel obstruction in pregnancy is 3.4% [5] which is high compared to the general population because pregnancy is a short period. The risk in pregnancy is doubled, with no increase in the first trimester, 2× in the second, and 3.2 in the 3rd. In Sweden, an 11-fold increased risk of undergoing diagnostic laparoscopy or laparotomy during pregnancy (from 0.1% to 1.5%) was found compared to women with BMI >35 kg/m<sup>2</sup> [7]. The mode of delivery does not depend on the type of prepregnancy bariatric procedure [8].

Small bowel obstruction occurs during the first pregnancy after surgery in 76% [9] or a 34-fold (from 0.08% to 1.5% in Sweden) increased risk [7].

### 23.1.3 Prognosis

#### 23.1.3.1 Maternal Outcome

Maternal mortality is 2% [10–12]. Abdominal surgery was most common during the first pregnancy after bariatric surgery. Only 20% of women had additional pregnancies after having surgery or a diagnosis of intestinal obstruction during the first pregnancy [7]. Obesity during pregnancy is associated with many maternal complications, including gestational diabetes mellitus (GDM) and hypertensive diseases, including pregnancy-induced hypertension (PIH) [13], which can result in adverse maternal and neonatal outcomes along with prepregnancy bariatric procedures. Findings indicate a lower incidence of GDM and PIH in patients after bariatric surgery compared to the general population matched for prepregnancy BMI, age, and presence of prepregnancy comorbidities [14]. Interestingly, some patients with normal pregnancy weight gain after prepregnancy LSG developed GDM. The reason is unclear [8].

#### 23.1.3.2 Fetal Outcome

The fetal loss rate is 17% [10–12]. In addition, birth trauma, operative deliveries, Cesarean sec-

tions (CS), and congenital malformations are more likely in obese mothers [15, 16]. Therefore, weight loss before pregnancy is critical for improving maternal and fetal outcomes [17]. Although bariatric surgery improves outcomes [4], fetal development can be impaired after rapid weight loss and disruption of nutritional balance during pregnancy, increasing small for gestational age (SGA) infants (2.16×) but decreasing large for gestational age infants [14, 18]. Improved outcomes were also for intrauterine growth restriction (2.16×) and preterm deliveries (1.35×) [18], although some found a lower rate of preterm deliveries (different group comparisons) [14]. All maternal and fetal malnutrition consequences were observed in “malabsorptive” procedures rather than the “restrictive” such as LSG [19, 20]. A threefold increased risk for SGA after prepregnancy LSG challenges the presumption that the observed risk of impaired fetal growth is due to malabsorption [18] and suggests that the deleterious effect on fetal growth may involve factors other than malabsorption [21].

Mothers after prepregnancy RYGB, classified with obesity at conception, had obstetric and neonatal outcomes than women with prepregnancy BMI  $\geq 35$  kg/m<sup>2</sup> who had never undergone RYGB [22]. The worst fetal outcomes are seen after biliopancreatic diversion, which should be used selectively in patients wishing for more children [23]. The abortion rate after bariatric surgery is 23–26%, without the difference before and after 1 year of surgery [24, 25]. Although the gestational age at delivery is similar in mothers with or without maternal anemia, the neonatal birth weight in mothers with anemia is 300–400 g lower. Notably, mothers without anemia have a mean neonatal birth weight of 3037 g [8].

*The American Association of Clinical Endocrinology, the Obesity Society, and the American Society for Metabolic and Bariatric Surgery recommend waiting for 12–18 months [26]. The American College of Obstetricians and Gynecologists recommend 12–24 months [4] after surgery before conceiving.*

Pregnancy immediately after bariatric surgery could be compromised due to (1) early postoperative complications, (2) failure of the procedure, (3) minimal or no weight gain, and (4) too short period for metabolic adaptation, with an increased risk of anemia because of iron, folate, and vitamin B12 deficiencies [27, 28]. Vitamin B12 was low in 53.4%; folic acid in 16.1%, iron in 6.7%, ferritin in 41.7%, calcium in 16.7%, and albumin in 10.3% of the patients [24]. This leads to maternal anemia, one of the main causes of low birth weight [29].

BMI at conception decreases as the interval between LSG and conception increases. The pregnancy interval after LSG does not impact maternal or fetal complications or birth weight. In a paired comparison of pregnancies before and after LSG, birth weight and the number of SGA births were lower in pregnancies after LSG. LSG is associated with a delay in the onset of GDM. LSG does not affect the mode of delivery, but the CS rate is higher for deliveries after LSG [30]. Others confirmed no significant difference between groups conceived within or later than 12 months after bariatric surgery regarding GDM, preeclampsia, CS rate, and adverse neonatal outcomes [31]. This may be related to the lower maternal glucose levels seen in the bariatric surgery group [32]. Maternal weight loss surgery does not alter the fetoplacental circulation [32]. The CS rate is higher among women with RYGB than in the Danish background population (around 20%) [33]. Sheiner et al. in 2004 revealed a higher rate of CS after prepregnancy bariatric surgery [34].

There are three cases of bariatric surgery during incidental pregnancy. Two cases after LSG had normal fetal development and delivery [35, 36]. The third patient, after RYGB, decided to terminate normal pregnancy [37].

### 23.1.3.3 Breastfeeding

Breast milk of women after prepregnancy bariatric surgery appears to be adequate in energy, macronutrients, and vitamin A during the first 6 weeks of lactation. This supports the conclusion that breastfeeding should not be discouraged in this group [38]. No data exist about mothers'

milk composition after emergent small bowel resections during pregnancy. Enteral or parenteral nutritional supplementation is essential.

## 23.2 Intussusception

### 23.2.1 Incidence

After laparoscopic RYGB (LRYGB), 0.1–0.3% of the patients in the general population will develop an intussusception [39], while the percentage after LRYGB during pregnancy is unknown. Post-LRYGB intussusception can be antegrade or retrograde. Retrograde intussusception is the more common mode of intussusception in the pregnant [40] and nonpregnant [41]. Up to 2019, 22 cases of pregnancy were published. At least 17/22 invaginations were retrograde, and at least 15/22 of the invaginations were located at the jejunojejunostomy [40]. Wax et al. described the first retrograde jejunojejunal intussusception in pregnancy in 2007 [42]. Retrograde jejunojejunal intussusception after LRYGB during pregnancy could have a higher incidence than in the general population.

### 23.2.2 Pathophysiology

See Sect. 18.2.3. Retrograde (antiperistaltic) intussusception is rare but the most common after RYGB in the general population. The incidence is 0.07–0.15% after both LRYGB and open RYGB (ORYGB) [43, 44]. Although retrograde peristalsis occurs naturally in the intestinal system, retrograde intussusception does not. There are several theories of intussusception. One theory includes an iatrogenic lead point—variations in the configuration of jejunojejunostomy, i.e., antiperistaltic versus isoperistaltic, or the use of staplers or suture lines. The entry point is just below the jejunojejunostomy, and there is a characteristic absence of any identifiable leading point. An iatrogenic lead point created by the suture or staple line at the enteroenteral anastomosis may generate hyperperistalsis of the excluded segment, causing the biliopancreatic

limb to telescope into the common limb [44, 45]. Postoperative adhesions could also be the cause. Roux stasis syndrome is another possible etiology. Hocking et al. developed a theory of dysmotility of the Roux limb in 1991. Disordered peristaltic activity in the Roux limb could create adjacent areas of high and low pressure, thus allowing for an intussusception. Potential confirmation is the absence of intraluminal, intramural, or extraluminal cause for the retrograde jejunojejunal intussusception (Fig. 23.1). Irregularities in the pacesetters distal to the jejunojejunostomy anastomosis may result in atony and distension of the Roux limb, with associated antiperistaltic movement distal to it [46, 47]. Most intussusceptions complicating RYGB occur in a retrograde fashion, supporting this theory. Further confirmation is intraluminal manometry in RYGB patients with recurrent intussusceptions showing abnormal intestinal motility [48].

Pregnancy increases intra-abdominal pressure with the pushing effect on intestinal loops, increasing the risk of intussusception, with the relaxing effect of progesterone on bowel motility [42]. RYGB-induced weight reduction can generate an attenuated thin mesentery prone to twisting or intussusception. The period between prepregnancy LRYGB and intussusception is 1–9 years [49, 50]. Daellenbach et al. showed that 98.4% of the intussusception cases occurred in women [51]. This could be due to hormonal factors.

### 23.2.3 Clinical Presentation

See Sect. 18.2.5.

### 23.2.4 Differential Diagnosis

The nonspecific nature of abdominal complaints early in RYGB-associated obstruction may incorrectly be attributed to common obstetrical complaints such as morning sickness, hyperemesis, reflux, and uterine contractions. Due to upper abdominal pain, other gastrointestinal diseases are often suspected, such as acute pancreatitis, acute cholecystitis, and even acute appendicitis.

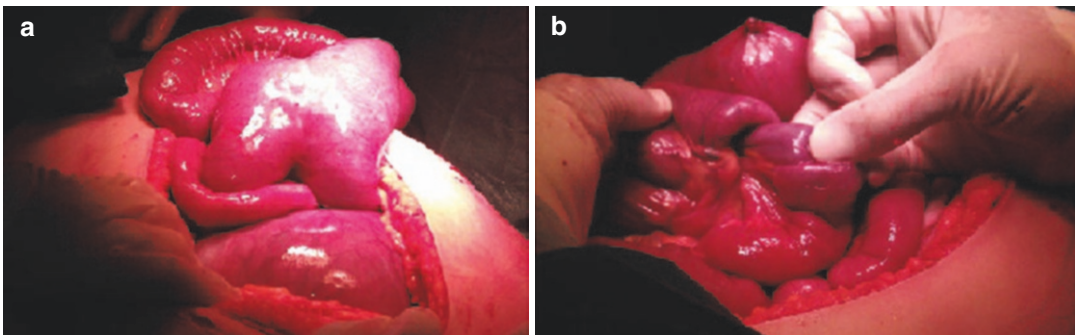
### 23.2.5 Diagnosis

#### 23.2.5.1 Plain Abdominal X-Ray

Plain abdominal radiograph findings depend on the degree of intestinal obstruction. With complete obstruction, air–liquid levels are present as in any other cause of intestinal obstruction. Unfortunately, misleadingly normal findings are common with retrograde intussusception after RYGB [49].

#### 23.2.5.2 Transabdominal Ultrasound

Transabdominal ultrasound was used in 50% but was rarely diagnostic [52]. At least in a significant proportion, there is a high-grade suspicion of small bowel obstruction [53, 54]. The classic



**Fig. 23.1** Dilation of the small bowel, including the anastomosis. (a) The gravid uterus is seen in the lower part of the laparotomy exposure. (b) Manual reposition of

retrograde jejunojejunal intussusception. (Reproduced with permission from [50])



appearance is a peripheral hypoechoic ring (*the target sign*) with central echogenicity (*the pseudokidney sign*). These correspond to the bowel wall surrounding hyperechoic mesenteric fat within the intussusception. Also, the vascularization of intussusciens can be estimated [52]. The advantage of this technique is the additional evaluation of the fetal status.

### 23.2.5.3 Abdominal CT

Abdominal CT can reveal small bowel distension proximal to the jejunojejunostomy anastomosis, with distension of the gastric remnant. The classic *target sign* suggests an intussusception distal to the jejunojejunostomy (Fig. 23.2a). Pneumatosis of the intussuscepted bowel indicates bowel ischemia, probably with gangrene (Fig. 23.2b).

### 23.2.5.4 Abdominal MRI

The transabdominal US is rarely diagnostic, and patients should undergo an abdominal MRI, which accurately reveals *telescopic sign* and *target sign*, typical for intussusception (Fig. 23.3).

## 23.2.6 Gastrosocopy

Surgical intervention of IH or intussusception is indicated when gastroscopy discards the stenosis of gastrojejunostomy [56, 58] or confirms

ischemia/necrosis of the small bowel mucosa [58, 59].

## 23.2.7 Treatment

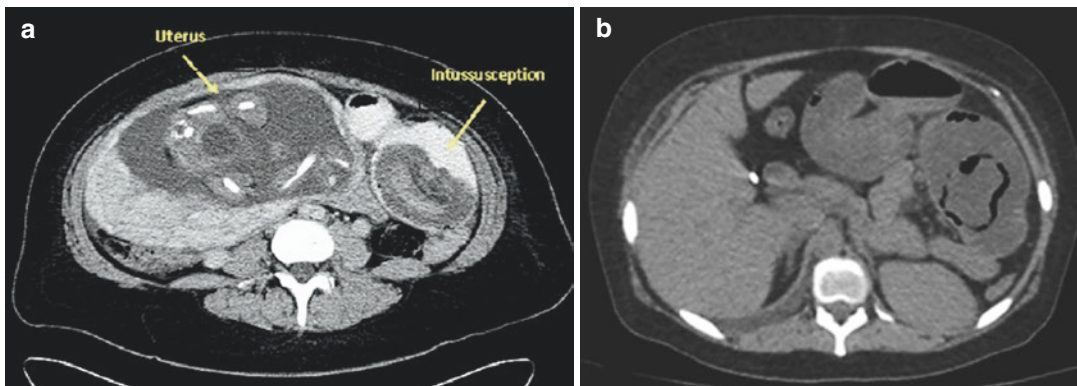
Abdominal complaints otherwise considered benign in pregnant patients should lower one's threshold to consult a bariatric surgeon if there is a history of RYGB. Likewise, the suspected intestinal obstruction should indicate a low threshold for exploration of the pregnant patient after RYGB.

Blind nasogastric tube insertion is contraindicated in RYGB patients. It can result in bowel perforation at the gastrojejunostomy and a false sense of decompression. At the same time, the biliopancreatic limb can remain obstructed.

No consensus exists on the optimal surgical technique to reduce intussusception in pregnancy after pre-pregnancy RYGB.

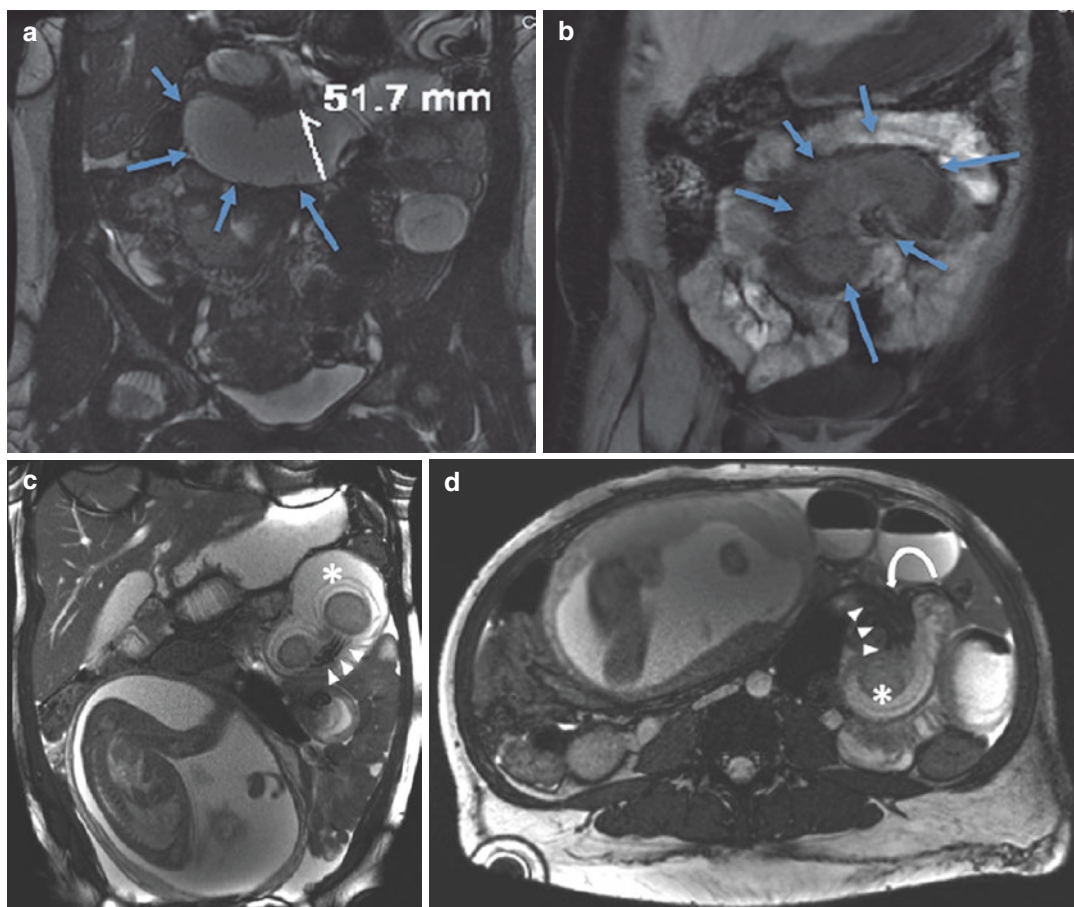
### 23.2.7.1 Retrograde Intussusception

Manual reduction is the simplest and most effective option that can be done laparoscopically. Unfortunately, the method is successful in 23% [40]. 45° angled laparoscope is used with two 5-mm ports in the upper left abdomen (Fig. 23.4)



**Fig. 23.2** (a) Abdominal CT at 33 weeks of pregnancy shows the *target sign* suggesting an intussusception distal to the jejunojejunostomy. (Reproduced with permission from [55]); (b) Axial native-CT shows an aerial image in

a halo, which could correspond to pneumatosis and parietal swelling, compatible with jejunojejunal invagination. (Reproduced with permission from [56])

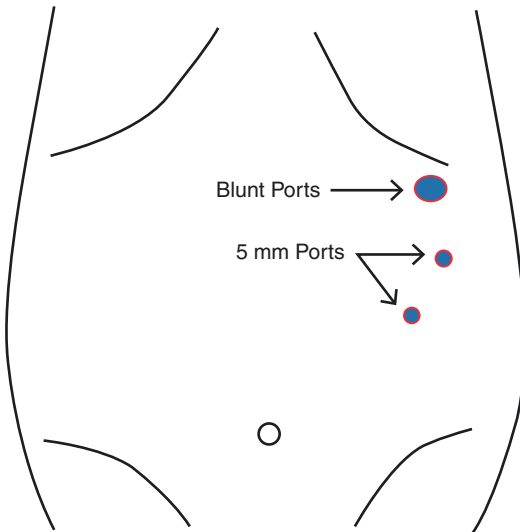


**Fig. 23.3** An abdominal MRI shows first-trimester small bowel intussusception. The *telescopic sign* is seen on the coronal views, (a) and (c). (Reproduced with permission from [54]). The *target sign* is seen on both axial and sagittal views, (d) and (b), respectively. (b) Marked jejunal dilation with submucosal edema in a bowel-within-bowel

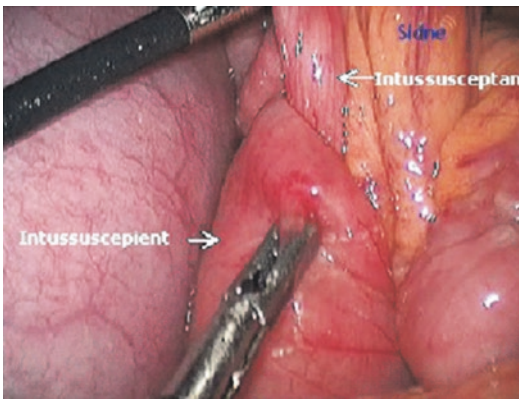
configuration (\*) centered by mesenteric vessels (arrowheads) and intrauterine pregnancy; (d) mesentery (arrowheads) entering into the jejunum (\*). A curved arrow marks the entry point. (Reproduced with permission from [57])

or right abdomen [53]. With an enlarged gravid uterus, the distended bowel occupies most of the upper part of the abdomen. Because the distended bowel is more challenging to manipulate and is prone to unintentional injury, the exploration starts on the decompressed bowel. The patient is placed in a Trendelenburg position with her body tilted to the left for vena cava decompression. The terminal ileum should be identified, and the bowel examined in a retrograde fashion [55, 56] until the point of a retrograde intussusception is reached (Fig. 23.5). Distal to the intussusception, the bowel is collapsed, while the proximal bowel

is distended and edematous. The intussusception is stabilized, and the intussusciens is gently pulled away (Fig. 23.5). Initially, some resistance to the reduction is felt. However, with slow and gentle pulling, the intussusciens bowel is reduced. It is inspected for signs of ischemia or perforation. The bowel can be edematous and congested but viable. The exploration should not be complete unless other sources of obstruction, such as IHs or adhesions, have been ruled out [60]. Thus, the Roux limb and biliopancreatic limb are also examined. The jejunojejunostomy, Peterson's defect, and the transverse mesocolon



**Fig. 23.4** Two 5-mm ports are placed in the upper abdomen in line with the camera to start the exploration from the distal collapsed small bowel in a retrograde fashion. (Reproduced with permission from [55])



**Fig. 23.5** Bowel is examined in a retrograde fashion from the terminal ileum until the point of retrograde intussusception is reached. (Reproduced with permission from [55])

window are inspected. Some claim this technique has no recurrence in the general and pregnant population [55]. Enteropexy with nonabsorbable sutures was not described in pregnancy.

With the failed manual reduction, surgical treatment involves resection of jejunojejunostomy and reconstruction of a new jejunojejunostomy distally. It was indicated in 77% of patients [40]. Despite this, recurrences can occur. To pre-

vent jejunal intussusceptions after RYGB, LSG could be a better option for pregnant patients or those who want to become pregnant [45].

### 23.2.8 Prognosis

Obesity during pregnancy might be associated with a higher risk of fetal malformations like neurological defects, congenital heart defects, orofacial clefts, and anorectal atresia [61]. Offspring of women after bariatric surgery are at an increased risk for long-term pediatric endocrine [62] and hematologic [63] morbidity. The fetal complication rate could be higher in patients with the antepartum complication of bariatric surgery.

#### 23.2.8.1 Maternal Outcome

The maternal survival is 100% [40]. Despite common segmental bowel ischemia, bowel perforation with peritonitis did not develop. The obstruction is commonly not so severe as to cause severe volume and electrolyte disturbances.

#### 23.2.8.2 Fetal Outcome

Fetal survival is excellent, around 95% [40]. Only one fetal death (one of the twins at 25 weeks spontaneous vaginal delivery due to complications of necrotizing enterocolitis) has occurred [64].

## 23.3 Incarcerated Internal Hernia

### 23.3.1 Classification and Pathophysiology

An incarcerated IH occurs in 5% of patients after LRYGB for morbid obesity in the general population [65]. This rate is higher with the open approach. It is attributed to greater adhesion formation that tethers and immobilizes small bowel loops, preventing their passage through surgically created mesenteric defects [6, 66–68]. Modifying the initial bypass procedure to lower the risk of subsequent IHs is ineffective. For instance, although it has become common to

suture all mesenteric defects at the time of initial surgery, the rapid postoperative weight loss predisposes to a widening of suture lines and reopening of these defects [1, 2, 68].

The most common site of IH after LRYGB is a surgical defect in the transverse mesocolon, created using a retrocolic approach for the anastomosis between the Roux limb and gastric pouch. An antecolic approach eliminates the creation of such a defect. It remains possible for the small bowel to herniate through a surgical defect in the small bowel mesentery or a defect between the Roux limb mesentery and the transverse mesocolon, constituting a so-called *Petersen's hernia* (Fig. 23.6).

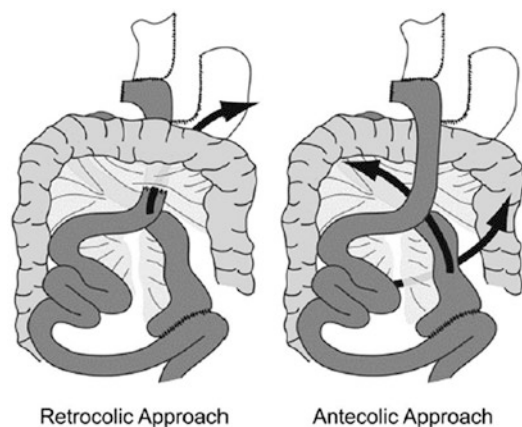
Over 80% of RYGB surgeries in the USA are performed in female patients [69], frequently of childbearing age [2, 66]. The significant weight loss after surgery improves fertility and increases sexual activity, increasing the pregnancy rate in patients with a history of RYGB [2, 66, 68, 70].

Several factors predispose to IH during pregnancy after prepregnancy RYGB [1, 2, 66, 68, 72] as follows:

- Laparoscopic approach—more difficult closure of potential spaces/defects created during the procedure,
- Increased intra-abdominal pressure, pronounced in advanced pregnancy,
- Pushing effect of the gravid uterus on intestinal loops,
- Marked prepregnancy weight reduction generating a significant intra-abdominal fat loss which can widen potential spaces/defects.

### 23.3.2 Incidence and Risk Factors

In 2004, Moore et al. provided the first report of a transmesenteric IH after RYGB in pregnancy [70]. The prevalence of IH in pregnancy after RYGB goes up to 8% [24]. IH to intussusception ratio in pregnancy after prepregnancy RYGB is 4:1 [73]. Most cases are in advanced pregnancy; 2/3 of patients are in the third, and others are mainly in the advanced second trimester [73–75]. The average gestational age is  $29 \pm 5$  (range, 6–37.43 week) [76]. The average RYGB to IH interval is  $2.65 \pm 1.98$  years (range, 5 month to 9 year) [76]. The possibility of developing an IH after RYGB is lifelong [2]. The average weight loss is  $46 \pm 15$  kg (range, 18–78.81 kg) [76]. Almost 50% [1, 66, 72, 77, 78] occurred within a year of RYGB. The mean BMI was 24–25 kg/m<sup>2</sup> [75, 76]. LRYGB was performed in 92% [76].



**Fig. 23.6** Diagram of the IHs after LRYGB. An IH through the transverse mesocolon defect is the most common after LRYGB but only with a retrocolic approach. With an antecolic approach, the small bowel can herniate through the space between the Roux limb mesentery and the transverse mesocolon (*Petersen's hernia*) or the surgically created small bowel mesenteric defect. These later two IHs are uncommon with a retrocolic approach. (Reproduced with permission from [71])

Women should postpone pregnancy for at least 1 year after RYGB to allow for complete wound healing and weight stabilization to avoid the most critical period for early postoperative IH [1, 2, 66].

The antecolic approach was made in 62% and retrocolic in 38% [76]. Petersen's hernia accounts for 57.4% (100% with antecolic approach [75]), jejunojejunal defect 46.3%, and transverse mesocolic defect 1.85% [76]. Petersen's hernia occurs mainly in the third trimester than in the second and infrequently in the first trimester [64, 68, 79].



There is a potential for a decline in the IH rate during pregnancy. First, surgeons started to close the mesenteric defects after RYGB when this issue was encountered. For example, the mesenteric defect closure in Sweden started in 2012 [7]. A review of English language cases since 2004 revealed that closure of mesenteric defects during RYGB surgery was performed in 8.5% [76]. Second, LSG has been increasingly used due to its technical simplicity and similar efficacy, eliminating the risk of IH formation, marginal ulcer, and gastrogastic fistulae after RYGB. Unfortunately, no difference in IH rate was observed whether the mesenteric gap was closed or not [5].

### 23.3.3 Clinical Presentation

The duration of symptoms before visiting the emergency department is 20 h [75].

IH in pregnancy is challenging to diagnose clinically, given the nonspecific and often subtle presentation. Upper abdominal pain complicates 10% of pregnancies with prepregnancy RYGB; in two-thirds, the pain could result from IH [33]. The presenting symptoms are often vague, ranging from cramps to severe abdominal pain. Epigastric pain is present in 52.5%, diffuse pain in 25%, left upper quadrant pain in 17.5%, and left-sided pain in 7.5% [76]. Patients with severe epigastric or periumbilical pain, initially cramping, seek to find a position of comfort, either leaning forward or on their side. Patients typically have nausea and retching. Blood pressure is usually normal, but the pulse is elevated [80]. Once it occurs, the obstructed afferent limb of the duodenum presents no typical symptomatology suggestive of intestine obstruction [78]. Therefore, the progression from obstruction to strangulation and ischemia develops. In these cases, bloody vomitus can be present. Nausea and vomiting are present in 70%, hematemesis in 8%, and bloody diarrhea in 5% [76].

A gynecological examination reveals normal findings [80].

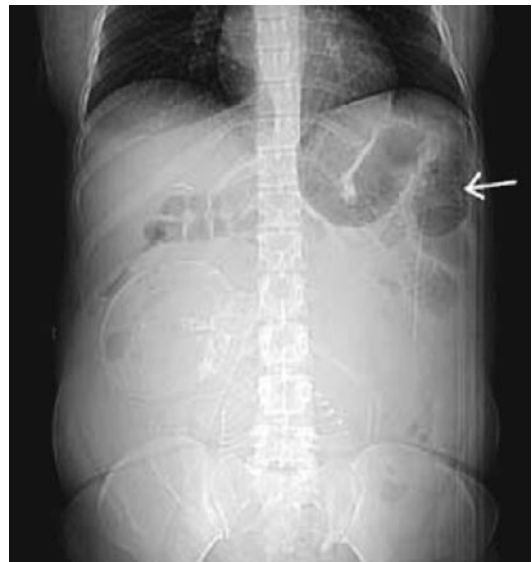
### 23.3.4 Diagnosis

#### 23.3.4.1 Laboratory Findings

Leukocytosis is present in 31%, and elevated serum lactate levels in 10% [76]. Hence, leukocytosis and elevated serum lactate should not be used as markers for IH. An explanation could be that multivisceral involvement and ischemia need to occur to increase systemic lactate. Furthermore, the amount of released lactate from ischemic bowel regions must exceed the liver's metabolic capacity. Some patients have elevated serum amylase levels, misdiagnosing them as acute pancreatitis [81].

#### 23.3.4.2 Plain Abdominal X-Ray

Plain abdominal X-rays are performed in 13% [76]. Typical signs of obstruction, such as air–fluid levels or dilated bowel loops, are often absent, therefore misleading. A closed-loop obstruction with a cluster of small bowel loops, mainly in the left upper quadrant, can be visualized (Fig. 23.7). In the general population, plain abdominal X-ray or contrast studies are negative or nondiagnostic for bowel obstruction or IH up to 20% [82].



**Fig. 23.7** A closed-loop obstruction with a cluster of small bowel loops in the left upper quadrant (white arrow) in 32 weeks of pregnancy. (Reproduced with permission from [68])



### 23.3.4.3 Abdominal CT

Abdominal CT has high accuracy for diagnosing an IH after RYGB [67, 83]. In 50% [2, 66, 68, 69, 72], CT appearance of an IH was demonstrated. In an additional 25%, CT findings assisted in the diagnosis [1, 78]. The CT findings include an abnormal cluster or swirling (Fig. 23.8) of small bowel loops and displacement, engorgement, and stretching of the mesenteric vessels [83]. The IH should be suspected with small bowel loops in nonanatomical positions, such as the lesser sac [66] or a dilated gastric pouch (Fig. 23.9).

An abdominal CT with oral and IV contrast accurately evaluates RYGB patients with obstructive symptoms of IH. The interpretation of the CT by an experienced bariatric surgeon and radiologist experienced in bariatric patients can often diagnose the altered anatomy of an IH [67]. CT has a high degree of false-negative and false-positive findings in patients with a history of RYGB. Furthermore, displaced intestines in advanced pregnancy make the interpretation more challenging. Even in nonpregnant patients, the sensitivity of detecting IH is 85% [84].

### 23.3.4.4 Abdominal MRI

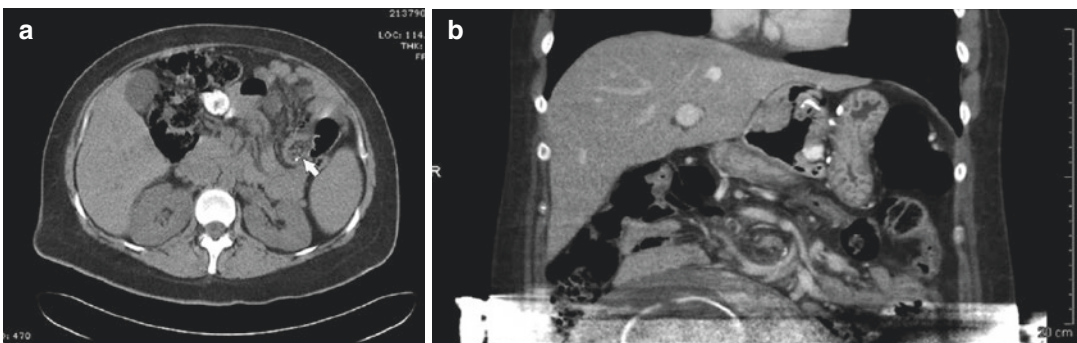
Until 2020, only 5% were diagnosed by MRI [76]. The various findings identified on MRI match the previously reported CT findings of an IH [83]. It seems reasonable that MRI could have utility in establishing the diagnosis of an IH;

however, MRI cannot replace CT for this diagnosis in all cases. For instance, the only suggestive findings may involve changes in the mesenteric vasculature, which an unenhanced MRI would not optimally assess. Furthermore, MRI may not be widely available on an emergent basis. CT remains an option in cases where MRI cannot be performed, or the diagnosis remains equivocal after MRI.

MRI should be considered when evaluating a pregnant patient with a history of RYGB who presents with abdominal pain. Mesenteric swirl (*whirl sign*), superior mesenteric vein beaking, mesenteric vascular congestion, and mesenteric edema have good to the excellent interobserver agreement for diagnosing IH in pregnancy (Fig. 23.10). The other evaluated signs (*hurricane eye sign*, clustered small bowel loops, *mushroom sign*, small bowel posterior to the superior mesenteric artery, crisscrossing of vessels, dilated gastric remnant, right-sided jejunal anastomosis, and small bowel obstruction) had a poor interobserver agreement or low diagnostic accuracy [86].

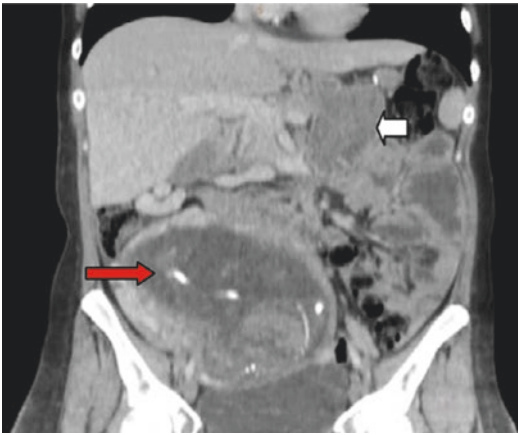
### 23.3.4.5 Gastroscopy

The diagnosis of IH or intussusception is an indication for the operation when gastroscopy discards the stenosis of gastrojejunostomy [56, 58] or ischemia/necrosis (Fig. 23.14) of the small bowel mucosa [58].



**Fig. 23.8** Abdominal CT of internal hernia. (a) Axial image at 25 weeks pregnancy. (Reproduced with permission from [72]) and (b) coronal image at 30 weeks preg-

nancy show swirling of twisted small bowel mesentery (arrow). (Reproduced with permission from [85])

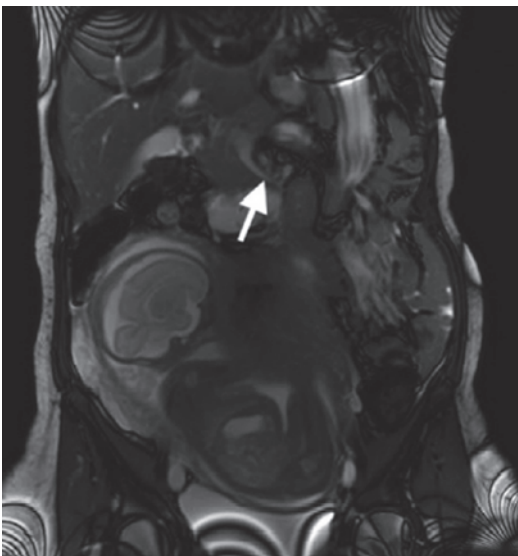


**Fig. 23.9** Abdominal CT shows gravid uterus (red arrow) and dilated gastric pouch (white arrow) at 24 weeks pregnancy, 9 years after open retrocolic, retro-gastric Roux-en-Y gastric bypass. (Reproduced with permission from [2])

to rule out preoperatively [60]. The risk of relapse of IH after the previous closure of mesenteric defects in pregnant women may be explained by slippage of the closure. Therefore, IH remains an important differential diagnosis, even in patients with previous closure of herniation sites [33].

### 23.3.6 Treatment

A delay between the onset of obstructive symptoms and surgery during pregnancy over 48 h increases complications, including bowel incarceration, ischemia, gangrene, sepsis, and death [1, 66, 79, 87].



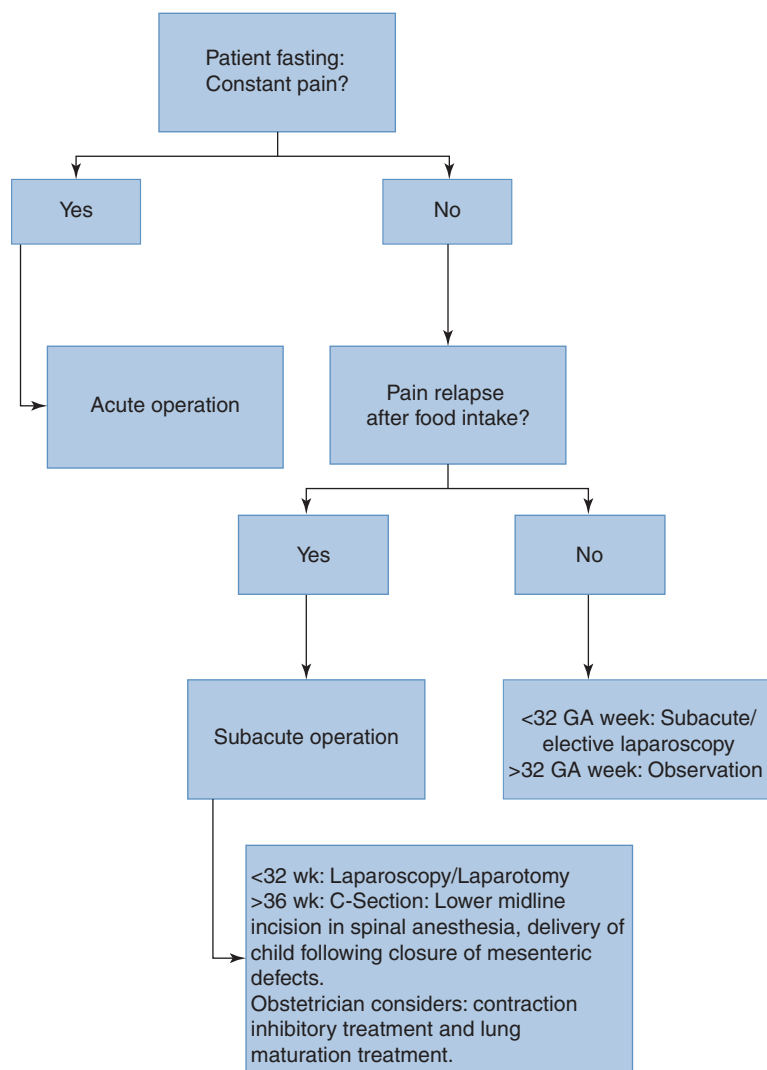
**Fig. 23.10** Magnetic resonance imaging of an internal hernia at 35-week gestation after antecolic laparoscopic Roux-en-Y gastric bypass. The white arrow shows the whirl sign. (Reproduced with permission from [75])

### 23.3.5 Differential Diagnosis

Laboratory findings are not diagnostic. The initial diagnosis could be acute appendicitis [75], gastritis, peptic ulcer perforation, acute cholecystitis, or acute pancreatitis. Adhesions are difficult

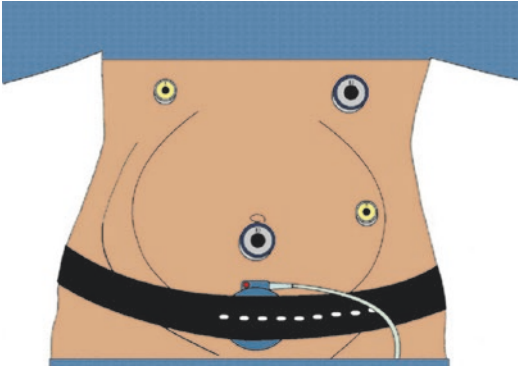
If emergent abdominal CT or MRI cannot be performed, there should be a low threshold to proceed to diagnostic laparoscopy/laparotomy based on clinical symptoms. Diagnostic laparoscopy is possible up to the 31st gestational week [74]. The diagnostic–therapeutic algorithm is presented in Fig. 23.11.

The laparoscopic approach is favored over the open approach when CS is not indicated [74]. Conversion to an open approach is 17–20% [73, 74, 88]. Slight variations in trocar placement exist [66], with the common position presented in Fig. 23.12. Laparoscopic reduction of IHs can be difficult, especially with dilated loops of ischemic or edematous bowel (Fig. 23.13). Running the bowel from the terminal ileum in a retrograde fashion may facilitate reduction [72, 85, 89]. With gangrenous changes, segmental resection with anastomosis is indicated [81]. If a long limb is gangrenous, resection should be followed by a new gastroenterostomy and jejunojejunostomy or a reversal of RYGB (Fig. 23.14). Reversal of the RYGB is indicated if BMI has normalized before pregnancy and due to the risk of metabolic disorder after resection of >1 m of the small bowel [59]. Strangulation with small bowel gangrene is common in the third trimester, partly due to the highest intra-abdominal

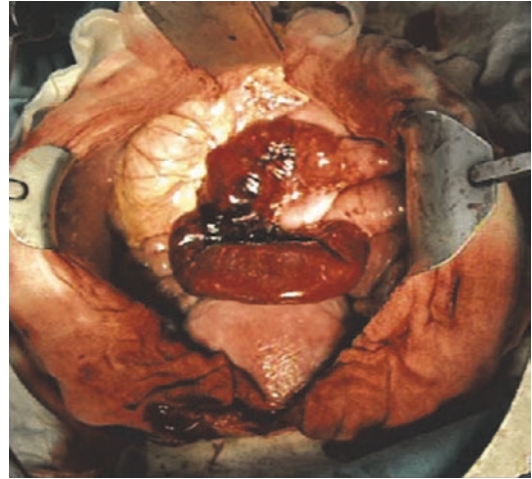


**Fig. 23.11** Flowchart for handling pregnant women with suspicion of internal hernia after Roux-en-Y gastric bypass. (Reproduced with permission from [74]. GA gestational age)

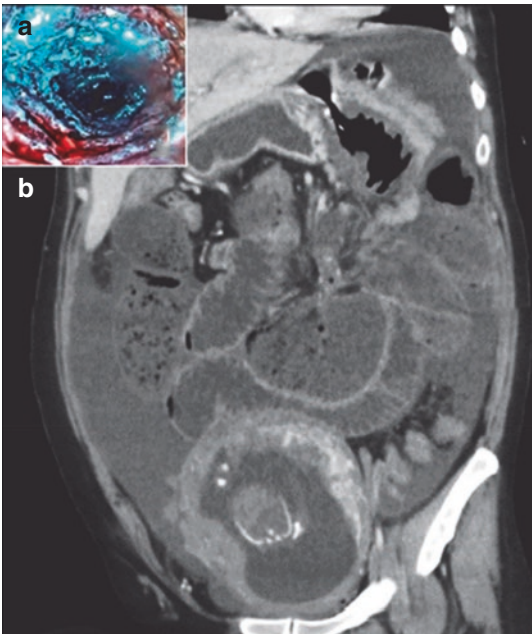
pressure in the third trimester. Moreover, due to the high fetal survival rate and the possibility of simultaneous CS, an exploratory laparotomy is the most common in the third trimester.



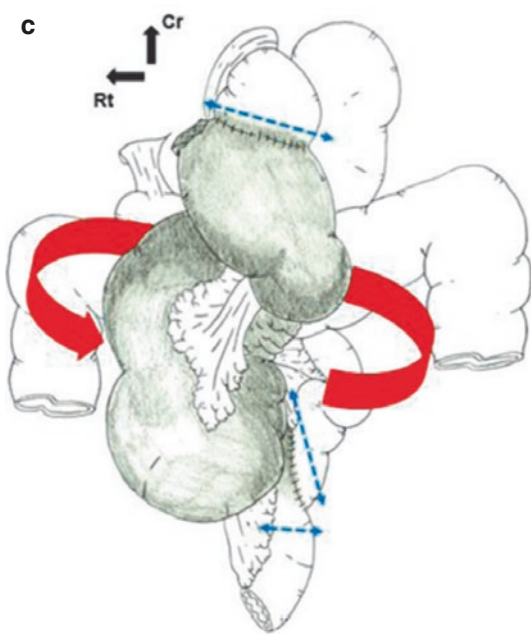
**Fig. 23.12** Trocar placement for laparoscopic repair of an IH during pregnancy after prepregnancy Roux-en-Y gastric bypass. (Reproduced with permission from [85])



**Fig. 23.13** After Cesarean delivery, an exploratory laparotomy demonstrated a gangrenous upper jejunum due to a fibrous band involving the afferent limb near the Roux-en-Y anastomosis. Segmental resection of the nonviable bowel followed. (Reproduced with permission from [77] under the CC Attribution License)



**Fig. 23.14** Roux limb strangulation through Petersen's space. (a) Endoscopic view showing necrosis of the gastrojejunostomy. (b) Abdominal CT shows Roux limb occlusion, with ischemic signs and some fluid. (c)



Schematic view shows the Roux limb strangulation through Petersen's space and the margin resection (*blue lines*). *Rt* right, *Cr* cranial. (Reproduced with permission from [59])

### 23.3.7 Prognosis

#### 23.3.7.1 Maternal Outcome

Up to 2020, maternal mortality from incarcerated IH after RYGB was <11%, mainly as a consequence of gangrenous bowel [76] or therapeutic delay of >24 h [88]. Recent series claim 0% mortality [73–75, 90]. The CS group had a median postoperative stay of 6.5 days, whereas the non-CS group had a median postoperative stay of 2 days [74].

#### 23.3.7.2 Fetal Outcome

A low threshold for imaging and surgical exploration in the pregnant population reduces fetal complications. Early exploration without bowel gangrene or perforation leads to normal pregnancy and fetal development. Fetal mortality increases with a therapeutic delay of >24 h [88]. Until 2020, fetal mortality was 14% [76], recently declining to 0% [74, 75, 90]. Overall and specific fetal morbidity is unknown. Almost all patients in the non-CS groups had term delivery of the live fetus [74, 88].

Prepregnancy bariatric surgery without proper counseling, medical supplementation, and avoidance of malnutrition, even without an acute abdomen, could lead to impaired fetal development [10]. Women of childbearing age after bariatric surgery should follow a well-balanced diet and supplements as part of a weight management strategy. Therefore, there is no reason to terminate a pregnancy during the first trimester [76].

## 23.4 Gastric Band Slippage

### 23.4.1 Incidence

Laparoscopic adjustable gastric banding (LAGB) was the second most frequent bariatric procedure, resulting in 17 cases requiring surgery, mainly for LAGB slippage [91]. The maternal weight and weight gain during pregnancy after prepregnancy LAGB were the highest compared to LSG and RYGB [8]. The *American Society for Metabolic and Bariatric Surgery* recommends that patients who become pregnant should have

band adjustments as necessary for appropriate weight gain to support neonatal growth [92].

LAGB slippage in pregnancy is 2.4–4% [93–95]. Several cases of gastric perforation after LAGB exist [96–98].

### 23.4.2 Pathophysiology

Direct gastric compression by the enlarging uterus distorts the stomach, which can predispose to band slippage. Additionally, the increase in intra-abdominal pressure, nausea, and emesis in early pregnancy can increase the rate of band slippage.

### 23.4.3 Clinical Presentation

The severity of gastric obstruction determines clinical presentation. With partial obstruction, vomiting is intermittent, while with progression to complete obstruction, vomiting becomes severe with signs of dehydration [99].

### 23.4.4 Differential Diagnosis

The differential diagnosis for LAGB slippage includes hyperemesis gravidarum, psychological factors, and viral gastroenteritis [99].

### 23.4.5 Diagnosis

In LAGB patients, a plain abdominal X-ray may help evaluate LAGB position and slippage. However, abdominal CT provides more detailed information about the perfusion or gastric torsion [91].

### 23.4.6 Treatment

To prevent band slippage, a gastric band is deflated, at least during the first trimester, for two reasons [99, 100]. First, if the patient develops hyperemesis gravidarum, band deflation mini-



mizes all band-related gastric complications. Second, it minimizes band slippage due to hyperemesis, the most common complication. If band slippage occurs, the only treatment is band removal, ideally by laparoscopic approach [99].

### 23.4.7 Prognosis

No low birth weight or congenital abnormalities were reported after pregnancy with prepregnancy LAGB [93–95].

## 23.5 Gastric Rupture

See Sect. 22.3.

## 23.6 Acute Cholecystitis

See Chap. 2.

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**Abstract**

Most surgical complications related to the spleen during pregnancy include severe intraperitoneal bleeding. The symptoms include acute and severe abdominal pain with progression to hypovolemic shock. Most patients do not have an underlying disease or similar symptoms previously. Without a history of abdominal trauma, abdominal sonography rarely finds the cause of free intraperitoneal fluid, while contrast-enhanced CT is diagnostic. Interventional radiologic techniques are increasingly used to stop splenic bleeding eliminating surgical and obstetric complications. Unsuccessful interventional radiologic techniques mandate emergent surgery. Exploration reveals a cause and allows definitive bleeding control. Splenectomy is most commonly performed for splenic rupture, splenic pregnancy, and splenic torsion. Due to earlier diagnosis and intervention, maternal and fetal mortality decreased to less than 10% and 40%, respectively.

diseased spleen. Eastman and Hellman made three important statements concerning the rupture of the spleen in pregnancy [1] as follows:

- The rarity of the condition,
- The danger of confusing it with obstetric complications,
- The importance of preexisting disease of the spleen.

Johannes Sylvester Saxtorph (Fig. 24.1), the Danish obstetrician, first described the splenic rupture during pregnancy in 1803 [2]. In 1866, Simpson referred to three cases of fatal splenic rupture, which had occurred respectively in the pregnant, parturient, and puerperal states. He pointed out the circumstance that, during pregnancy, there is often, if not generally, a kind of physiological leukocytosis. A certain amount of softening very frequently accompanies the hypertrophy of the spleen and predisposes it to laceration under vigorous exertion and muscular effort, blows, etc. [3]. One of the earliest cases was by Hubbard in 1879. However, the authenticity of this report is open to question as the findings are not recorded too clearly or soundly [4]. Kotschnew and Manankow gave the first overview of splenic rupture in 1930. An autopsy confirmed the first nine cases. In 1958, Sparkman provided an overview of 44 recorded cases, with a detailed analysis of their etiology [5]. In 1967, Buchsbaum added 27 cases to the list [6].

## 24.1 Splenic Rupture

### 24.1.1 Definition and Historical Perspective

Splenic rupture can occur with any degree of trauma to a normal spleen or minimal trauma to a





**Fig. 24.1** Johannes Sylvester Saxtorph, Danish obstetrician (1772–1840), first described splenic rupture during pregnancy in 1803. (Cropped picture from *Statens Museum for Kunst*, lithography by David Monies in 1835)

**Table 24.1** Pregnancy-related causes of splenic rupture.

| Etiology                   | Incidence (%) |
|----------------------------|---------------|
| Normal pregnancy           | 58            |
| Splenic ectopic pregnancy  | 24            |
| Post-vaginal delivery      | 5             |
| Post-caesarean section     | 5             |
| Preeclampsia               | 2.5           |
| Ruptured ectopic pregnancy | 2.5           |
| HELLP syndrome             | 2.5           |

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Literature up to 2003 indicates 18 more, bringing the total to 89 [7]. Classification is based on the cause [5] as follows:

- Traumatic,
- Following antecedent disease,
- Associated with toxemia of pregnancy,
- Spontaneous.

Incidence, according to the cause, is presented in Table 24.1.

## 24.1.2 Classification

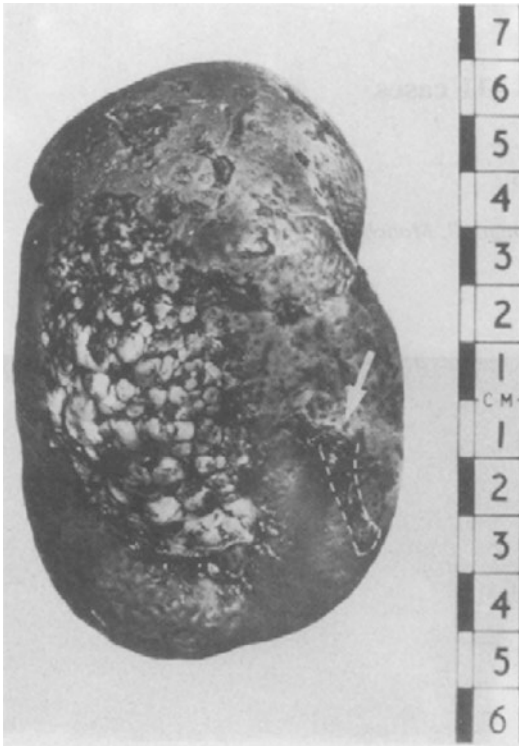
### 24.1.2.1 Trauma

#### Incidence

Thirty-five cases of traumatic splenic rupture in pregnancy are available. Probably some cases of spontaneous splenic rupture result from minor trauma of which the patients were unaware. Most cases result from road traffic accidents [9–13], rarely after bicycle falls [14], domestic violence [15], or even coitus [16]. Until 1988, a traumatic splenic rupture occurred in the third trimester in 48% of patients [17].

#### Etiopathogenesis

In its position behind the rib cage, cushioned under the left hemidiaphragm, the spleen is protected from most forms of direct trauma. Schamaun explained the pathogenesis of a rupture by a countercoup mechanism. Because of its relative mobility, the spleen is driven against the vertebral column and ruptures [18]. Another mechanism explains the rupture based on the ligamentous suspension of the spleen, which allows a limited degree of motion and then sudden fixation and laceration. Schonwerth described the deep inspiration at the instant of trauma (the fright mechanism) displacing the superior pole downward. In contrast, the lower pole is relatively fixed by the phrenicocolic ligament, causing flexion of the spleen. Trauma over the rib cage results in a capsular laceration on the stretched convex surface [19]. Sometimes underlying pathology and minor (repeating) trauma are unknown or unrecognized. In cases of the previously changed spleen or other pathology, even a minor or minimal but repetitive trauma is sufficient for splenic rupture. In one case, the prominent exostosis arising from the tenth rib had roughened and thickened a circumscribed area of the splenic capsule (Fig. 24.2) over the years due to the respiratory excursions and movement of daily life. Laceration of the unthickened lower pole occurs during pregnancy when splenic size, vascularization, and position may be altered [20]. In two cases, with the initial



**Fig. 24.2** Convex surface of the spleen shows the roughened capsule. The exostosis (*dotted outline*) has been replaced in the laceration (*arrow*). (Reproduced with permission from [20])

diagnosis of spontaneous splenic rupture, cavernous hemangioma of the spleen was the source of bleeding. It may be that minor trauma was the precipitating factor [21, 22].

Splenic trauma during delivery [23] could be a traumatic or spontaneous cause of splenic rupture (see Sect. 24.1.2.4), depending on the difficulties during labor and additional procedures.

#### 24.1.2.2 Toxemia of Pregnancy

Sparkman made the classification in 1958 because several cases were associated with toxemia of pregnancy [5]. The authors suggested that toxemia may be associated with specific conditions, such as hypertension, thrombosis, and diffuse angiitis, which may predispose to vascular or visceral rupture [24–28].

#### 24.1.2.3 Underlying Splenic Disease

The complete list of underlying causes of spontaneous splenic rupture is the same as in the nonpregnant population. It includes local splenic

disorders—splenic cysts and diffuse angiomatosis; hematologic diseases—hemophilia, congenital afibrinogenemia, and hemolytic anemia; metabolic disorders—amyloidosis, Wilson’s disease, Gaucher’s disease, and Niemann–Pick disease; drug-induced—intravenous heparin, warfarin, and streptokinase; iatrogenic—extracorporeal shock wave lithotripsy and clamping of the portal triad; and miscellaneous—vomiting, uremia, systemic lupus erythematosus, and other connective tissue diseases. Most notable are the infectious causes, such as infectious mononucleosis and malaria, considered the most common cause of spontaneous splenic rupture [29].

Cases associated with malaria [30], Banti’s syndrome [31], hemangioma [32], subacute bacterial endocarditis [33], leukemia and other blood-related disorders [34], and typhoid fever [35] have been reported. Buchsbaum reported spontaneous rupture in four cases—hemangiomas in two and splenitis in another two [6].

#### 24.1.2.4 Spontaneous Rupture of Normal Spleen

##### Definition

Some question the spontaneous rupture of the normal spleen [36]. Nelson and Hall reported a markedly diminished and almost total absence of germinal centers in the lymph nodes of pregnant women at term [37]. Of all cases of splenic rupture in pregnancy, only 2.2% were spontaneous in the puerperium [25]. In 1958, Orloff and Peskin established four criteria for the diagnosis of spontaneous rupture of a normal spleen [38], and Crate and Payne added the fifth criterion in 1991 [39] as follows:

- No history of trauma,
- No systemic disease that can affect the spleen,
- No evidence of perisplenic adhesions to suggest previous trauma,
- Splenic parenchyma, vasculature, and capsule normal macroscopically and histologically,
- Lack of viral infections related to the spleen.

A similar definition is by Sparkman [5]. More frequent examination of the surgical specimen will reveal pathologically changed spleens. The high incidence of secondary rupture indicates that as adequate histories are obtained and reported, more cases of minor trauma forgotten by the patient during the long latent period will be revealed [6]. It is likely that the so-called spontaneous rupture occurs due to capsular injury by the lower ribs from trivial blunt trauma (for instance, coughing and straining) either unnoticed by the patient at the time or forgotten in the light of subsequent events [38]. These factors will lower the number of cases designated as spontaneous rupture of the normal spleen in pregnancy. Sheehan and Falkiner, in 1948, analyzing 163 routine obstetric necropsies, found three clinical conditions for splenic enlargement (>200 g) in the second half of pregnancy [40] as follows:

- Severe anemia of pregnancy,
- Accidental hemorrhage of the abruption type,
- Puerperal thrombophlebitis or gross septic endometritis.

Splenic enlargement is a risk factor for splenic rupture.

### Incidence

Zuckerman and Jacobi collected 28 cases until 1937 and regarded 21 as spontaneous rupture of the normal spleen and 7 as doubtful [41]. Another 21 cases of spontaneous rupture of a normal spleen during pregnancy or labor have been reported in the English language literature between 1958 and 2011 [42]. However, a spontaneous rupture in pregnancy without antecedent trauma is rare and commonly occurs in the third trimester or puerperium [24, 42]. Until 1988, a spontaneous splenic rupture occurred in the third trimester in 60% of patients [17].

### Pathophysiology

The pathogenesis includes several mechanisms of rupture of the spleen [43] as follows:

- Local lesions as points of weakness,
- The increase of capsular tension due to hyperplasia and engorgement,

- Hypervolemic state,
- Diminished peritoneal cavity volume,
- Compression by the abdominal musculature,
- Increased intra-abdominal pressure.

However, the authors cannot postulate any theory about the etiology of spontaneous rupture of the normal spleen. Therefore, it is obvious that minimal internal trauma, such as straining for a bowel movement, coughing, vomiting, sneezing, jumping, or even coitus [44] in the latter stages of pregnancy, may be causally related to splenic rupture by increasing intra-abdominal pressure, transmitted to intra-abdominal organs. Also, the hemodynamic changes accompanying pregnancy may predispose to spontaneous splenic rupture via two possible mechanisms. First, the combined effects of the increased circulating blood volume and reduced volume of the peritoneal cavity due to the expansion of the gravid uterus with disturbance of the normal position of the spleen, mainly where the splenic pedicle is short, make the spleen more fragile and therefore more vulnerable to rupture [45]. In keeping with this hypothesis, it is interesting that almost all cases have occurred in multiple pregnancies or the third trimester. Secondly, circulating hormones such as estrogen and progesterone cause structural changes to the spleen that may increase the risk of splenic rupture during pregnancy, even after minor trauma [46]. In earlier works, pregnancy was thought to predispose the spleen to rupture. Therefore, pregnancy was listed as an etiological factor in splenic rupture. This view completely disregarded Barcroft's work, in which he demonstrated on a small number of dogs that the exteriorized spleen shrinks markedly during pregnancy [47]. Furthermore, the examination of the spleen at autopsy in eight pregnant female dogs with normal spleens failed to reveal any correlation between splenic weight and duration of pregnancy. Another widely held theory is that rupture of a small intrasplenic aneurysm may occur, with all traces of an aneurysm being destroyed by the bleeding, thus preventing its discovery by the pathologist.

### 24.1.2.5 Postpartum Splenic Rupture

#### Incidence

Only eight cases of spontaneous postpartum splenic rupture have been reported [24–28, 48]. Additional cases were during labor [2, 49].

#### Etiopathogenesis

The etiology of spontaneous postpartum splenic rupture remains speculative at best.

#### Splenic Enlargement

It has been suggested that splenic enlargement and increased blood volume typically seen in pregnancy, in addition to the trauma of parturition, could be implicated in the pathogenesis of splenic rupture (Fig. 24.3), but this is controversial.

#### Blunt (Internal) Trauma

Suggested etiological factors in cases of true spontaneous rupture include blunt internal trauma, as proposed by Barnett (i.e., occasioned by coughing, vomiting, coitus in the latter stages of pregnancy, and the bearing-down efforts of the second stage of labor) [23, 50]. Several authors have suggested a short splenic pedicle or deeply recessed location of the spleen as congenital factors that might contribute to rupture by compressing the diaphragm during coughing, sneezing, or vomiting [38]. Whether the episode of tonic-clonic seizure in one case

could be considered traumatic enough to induce injury to the spleen will remain unanswered [51].

#### Intrasplenic Aneurysm

Another widely held theory is that rupture of a small intrasplenic aneurysm may occur, with all traces of an aneurysm being destroyed by the bleeding, thus preventing its discovery by the pathologist (see Sect. 24.3).

#### Cesarean Section

At the operation, traction with undue force with sharp- or blunt-edged instruments during CS and inserting packs could cause abrasive injuries to an already congested organ such as the spleen, especially in previously operated patients with intraperitoneal adhesions. Excessive force in exploring the upper abdomen and manual expression of the fetus by forceful pushing on the upper abdomen at the time of CS or even while removing clots from the paracolic gutters might lead to splenic injury, especially in those with high blood pressure [48].

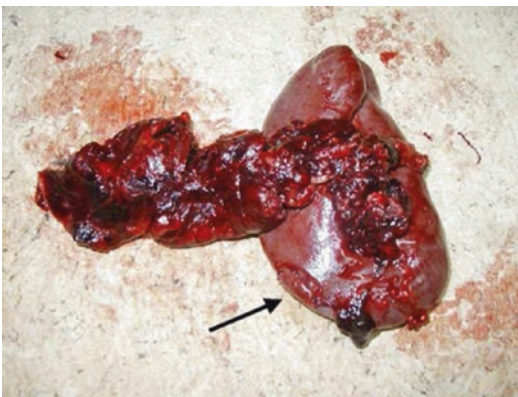
#### Rapid Plasma Expansion

It might also be possible that rapid plasma expansion with blood products and other volume expanders could result in a rapid volume increase within the spleen, predisposing it to rupture [51].

## 24.1.3 Clinical Presentation

### 24.1.3.1 Medical History

History of severe trauma with bony and soft tissue injury is frequently associated with intraperitoneal bleeding. The most common is a fracture of the ribs, which occurs in 35% of cases of traumatic splenic rupture in the general population. In some instances, the date of the accident may be remote from the time of admission and may, under some circumstances, be forgotten altogether. There is no history of trauma in approximately 40–50% of splenic rupture cases. In two cases, after sexual intercourse, abdominal pain started within hours [16].



**Fig. 24.3** Rupture of the splenic capsule (arrow) on the lower pole. (Reproduced with permission from [7])

### 24.1.3.2 Physical Examination

Rupture may become manifest as follows:

- *Immediately* following the trauma,
- *Delayed* and only recognized following a latent period.

The immediate rupture usually presents no problem in diagnosis. McIndoe first emphasized the delayed splenic rupture in the general population in 1932 [52]. He reported that the acute onset of symptoms of rupture must occur 48 h or later following the initial injury to be called *delayed* rupture. In many cases, the latent period exceeds 1 week.

*Kehr's sign* presents diaphragmatic irritation referred to the left shoulder tip region. Some claim it is almost pathognomonic when present with blunt abdominal trauma. Blood from any cause in the left subphrenic space causes positive Kehr's sign, most commonly with a splenic rupture and ectopic pregnancy. Kehr's sign is present in a minority of these patients.

The classic triad of epigastric pain, tenderness, and Kehr's sign after blunt abdominal trauma is characteristic of a ruptured spleen.

Pain and tenderness are common. Epigastric pain is the symptom most commonly and most consistently reported. In some cases, there is an associated episode of vomiting. The pain is made worse by coughing, deep breathing, and moving. At rest, the pain may be almost entirely relieved. The progressive severity of pain is common. In most cases, the pain tolerated at rest becomes more severe, and analgesic medication is requested. In a few cases, dyspnea is reported due to the expanding intraperitoneal mass, declining circulating blood volume, or loss of hemoglobin. Dullness on percussion over the left upper quadrant is an important sign. The enlarging uterus makes percussion and palpation of upper abdominal masses more difficult. Barnett states that in advanced pregnancy, the enlarged gravid

uterus does not give rise to *Ballance's sign* [50]. It is dullness to percussion in the left flank or left upper abdominal quadrant and shifting dullness to percussion in the right flank. The dullness in the left flank is due to coagulated blood, and the shifting dullness on the right in altering position is due to fluid blood. In later stages, the pain can become generalized, with distention and rigidity. Muscle spasm may not be present even in the presence of intraperitoneal blood. Eventually, more than half of the patients will suffer a hemorrhagic shock if the condition is left untreated [25]. Some authors have noted the confusing coexistence of hypertonicity of uterine muscle. Whether this is due to local peritoneal irritation is not known.

### Postpartum Splenic Rupture

Rupture of the spleen in the postpartum period poses a significant difficulty for early diagnosis because more common entities present similar clinical findings, especially early in the rupture phase. This differential diagnosis should be considered with external compression of the uterine fundus during vaginal delivery.

### 24.1.4 Differential Diagnosis

In the first trimester, spontaneous splenic rupture is usually confused with ruptured ectopic pregnancy (Table 24.2). In the last trimester, the two most likely differential diagnoses are placental abruption and rupture of the uterus. However, in the case of splenic rupture, the uterus is not tender or hard, and fetal heart sounds can usually be heard (before hemorrhagic shock ensue).

During puerperium, differential diagnoses include exaggerated postpartum pains, uterine rupture, intra-abdominal bleeding in general, and injury of a viscus (Table 24.2).

### 24.1.5 Diagnosis

The true rate of preoperative diagnosis is unknown. One of the reasons for the complicated diagnosis is the unclear etiology of the rupture



**Table 24.2** Differential diagnosis of splenic rupture during pregnancy

| Traumatic       | Spontaneous                |                         |                        |                     |
|-----------------|----------------------------|-------------------------|------------------------|---------------------|
|                 | <i>First trimester</i>     | <i>Second trimester</i> | <i>Third trimester</i> | <i>Puerperium</i>   |
| Liver rupture   | Ruptured ectopic pregnancy |                         | Placental abruption    | Postpartum pain     |
| Uterine rupture |                            |                         | Uterine rupture        | Uterine rupture     |
| Renal rupture   |                            |                         | Acute pancreatitis     | Acute pancreatitis  |
|                 |                            |                         | Renal artery rupture   | Postpartum bleeding |

itself. The frequency of correct diagnosis during the 1950s varied between 14 and 25% [5, 53].

Perhaps the most confusing in the later months of pregnancy is the finding of uterine tetany, suggesting the strong possibility of placental abruption. Hemoperitoneum and peritoneal irritation may make adequate uterine palpation difficult, and auscultation of fetal heart sounds uncertain. Albuminuria may be present and add to the difficulty of distinguishing between intraperitoneal bleeding due to splenic rupture and placental abruption.

Diagnosis is frequently challenging because pregnancy leads the obstetrician to concentrate on the possibility of uterine or adnexal injury. The clinical symptoms and signs normally associated with intraperitoneal bleeding may be poorly defined. When blood is lost swiftly, and in large amounts, all the characteristic features of hypovolemic shock are recognized without difficulty; however, when blood loss is slower and smaller in quantity, the appropriate abdominal findings may be obscured. The diagnosis of spontaneous postpartum splenic rupture was not considered in either case preoperatively, even though there was no doubt about the need for immediate surgical intervention and transfusion. Symptoms and signs of severe shock might be mimicked by septic shock, amniotic fluid embolus, pulmonary embolus, cardiogenic shock, and disseminated intravascular coagulopathy.

#### 24.1.5.1 Plain Abdominal X-Ray

The radiographic examination is not of much value in diagnosing a spleen rupture. Careful observation may indicate the following:

- Elevation of the left hemidiaphragm,
- Displacement of the gastric shadow to the right,

- Subphrenic opacity in the left upper quadrant,
- The descent of the left part of the transverse colon.

These signs are less useful in the third trimester because of the enlarged uterus physiological displacement of intraperitoneal organs.

#### 24.1.5.2 Transabdominal Ultrasound

The transabdominal ultrasound (US) quickly confirms intraperitoneal fluid accumulation or hematoma. It can be performed at the patient's bedside or emergency unit [54]. US is an initial workup in hemodynamic instability and abdominal distention, especially if exploration is contemplated or CT is not feasible. Free fluid in the upper abdomen or left upper quadrant should raise suspicion of splenic rupture (see Sect. 25.3.7.3).

#### 24.1.5.3 Angiography

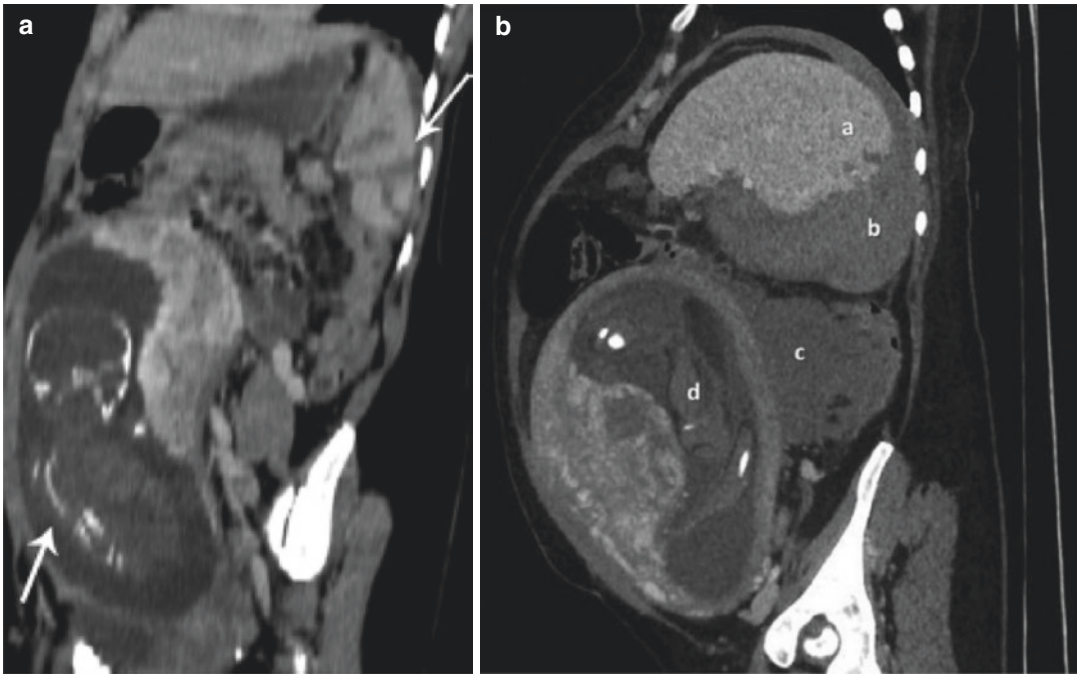
Preoperative diagnosis of splenic rupture or SAA rupture is mostly unrecognized. The gold standard for diagnosing suspected unruptured SAA is arteriography [55], although US and pulsed Doppler US are preferable in pregnancy [56].

#### 24.1.5.4 Abdominal CT

Angiography and contrast-enhanced abdominal CT defines SAA with or without rupture preoperatively but are rarely used in pregnancy. An abdominal CT is used when MRI is unavailable (Fig. 24.4).

#### 24.1.5.5 Paracentesis

Before US and CT, paracentesis was used to diagnose intraperitoneal bleeding. Wright and Prigot have strongly emphasized paracenteses in the four abdominal quadrants with a No. 18 needle; the blood was obtained in 87% of splenic



**Fig. 24.4** (a) An oblique sagittal CT image shows traumatic splenic laceration (*right arrow*) and the 26-week fetus (*left arrow*) [57]. (b) Parasagittal contrast-enhanced

CT shows spleen (a), subcapsular splenic hematoma (b), free peritoneal blood (c), and fetus (d). (Reproduced with permission from [58])

ruptures in the general population [53]. Dependence on paracentesis has been criticized with statements that false taps lead to dangerous, sometimes mortal delay [53]. A repeat paracentesis is mandatory if doubtful cases. An even better option is to proceed with laparotomy [53]. Currently, it is not used, especially in pregnancy, where there is an additional possibility of uterine and amniotic sac injury.

#### 24.1.5.6 Diagnostic Exploration

When the preoperative cause of bleeding is unknown, especially with hemodynamic instability, laparotomy is preferred. Laparoscopy cannot define and stop all causes of bleeding, especially in advanced pregnancy.

### 24.1.6 Treatment

#### 24.1.6.1 Historical Perspective

Savor, in 1898, performed the first splenectomy for a ruptured spleen in pregnancy [59]. The

patient survived and delivered a full-term infant 3 and half months later.

#### 24.1.6.2 Conservative Treatment

A conservative approach with close hemodynamic monitoring has been advocated in well-selected cases, most of which are traumatic in origin. There are no criteria or guidelines for pregnant patients, but to be eligible for nonoperative management, patients should meet several criteria based on data on the general population [60] as follows:

- Hemodynamic stability,
- The absence of peritoneal signs,
- The absence of other abdominal injuries requiring surgery.

Factors that predict the failure of conservative measures in the general population include [60] the following:

- Preexisting splenic disease,
- Age older than 55 years,
- High-grade injury,

- Significant hemoperitoneum,
- Contrast blush in the spleen (suggesting false aneurysms) on CT.

### 24.1.6.3 Surgical Treatment

#### Postpartum Splenic Rupture

The standard of care for patients with spontaneous postpartum splenic rupture remains emergency splenectomy. The survival rate of pregnant patients with splenic rupture who underwent splenectomy is 95.4%, compared to 0% without splenectomy [25].

The survival of patients with spontaneous postpartum splenic rupture rests on aggressive transfusion management, early diagnosis, and emergency splenectomy.

#### Operative Principles

A midline vertical incision is recommended to facilitate access, visualization, and CS. The problem is that the patient is often seen first by the obstetrician with a diagnosis of pelvic pathology. The most common incision is a lower midline or Pfannenstiel incision. In spontaneous rupture of the normal spleen, 75% resulted in splenectomy but through an inadequate incision [38]. Some patients needed extensions, some a new incision, and in the balance, the surgery was made extremely difficult by the original incision. The diagnosis of spontaneous postpartum splenic rupture was not considered in either case preoperatively, even though there was no doubt about the need for immediate surgical intervention and transfusion. Therefore, evaluation of the entire abdomen in posthysterectomy hemoperitoneum is advisable. CS with intraperitoneal bleeding from splenic rupture has two purposes as follows: (1) Adequate surgery for the ruptured spleen cannot be undertaken until the uterus is evacuated because a term-sized uterus prevents adequate exposure of the splenic fossa, and (2) CS prevents intrauterine death due to maternal hypoxia or hypotension.

#### Laparoscopic Splenectomy

The laparoscopic approach is extremely rare for traumatic splenic rupture [61, 62]. Laparoscopic procedures can be completed with early presentations during early pregnancy. Blood clots obscure the operative field with delayed presentation, making visualization difficult. Also, in hemodynamically unstable patients, definitive treatment must be swift; therefore, laparotomy is recommended.

#### 24.1.6.4 Endovascular Treatment

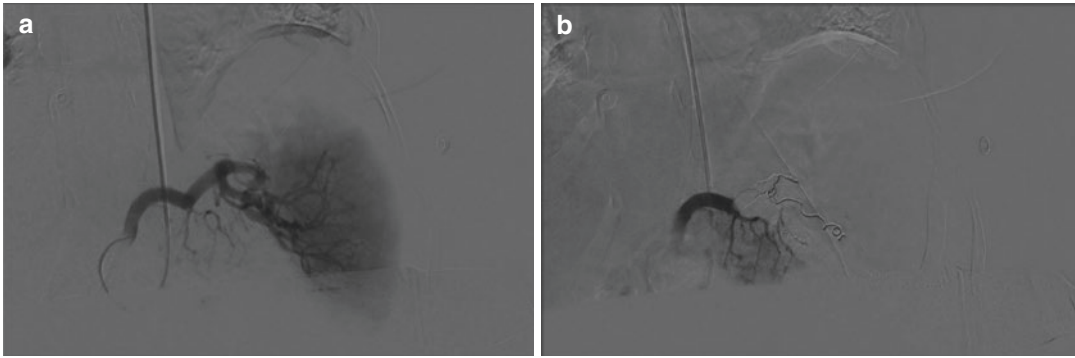
Splenic artery angiography followed by embolization in the general population has been described, with a reported success rate of 85% [63]. Endovascular assessment and management of splenic rupture are still unclear. Three cases have been described, and the treatment was successful [12, 58, 64]. Radial artery catheterization is minimally invasive, and coils deployed into the distal splenic artery distal to the origin of the greater pancreatic artery effectively stop the splenic bleeding (Fig. 24.5).

### 24.1.7 Prognosis

Due to the rarity, the maternal and fetal outcome for every etiology is difficult to estimate. Therefore, the outcome is mostly presented for all-cause splenic ruptures.

#### 24.1.7.1 Maternal Outcome

Maternal death is commonly due to massive bleeding and accompanying hemorrhagic shock and consumptive coagulopathy. Until 1880, the mortality was 100% [17]. With conservative treatment, the mortality was 100% [25]. Therefore, the maternal outcome depends on the duration from rupture to surgery. In 1952, Barnett stressed the severity of the condition with a maternal mortality of 54% [50]. Of all maternal deaths, 53% were recorded before 1880. Therefore, in the 1950s, maternal mortality was 35%. The mortality of patients taken to the operating room for splenectomy was 19% [5, 50]. Also, in the 1950s, the mortality from spontane-



**Fig. 24.5** Traumatic splenic rupture at 28 weeks gestation. (a) Pre-embolization angiography shows extravasation of contrast. (b) Postembolization angiography at the

level of the distal splenic artery without signs of bleeding. (Reproduced with permission from [64])

ous splenic rupture was 10% [38]. Up to 1967, maternal mortality was lowered to 8% [6]. With 20 cases in the English literature between 1958 and 2011, the maternal mortality from a spontaneous splenic rupture in pregnancy was 14.3% [42]. In two cases of emergent laparoscopic splenectomy, mothers survived [61, 62].

#### 24.1.7.2 Fetal Outcome

Maternal hemodynamic decompensation leads to an acute decrease in uteroplacental perfusion, resulting in “fetal distress” and, ultimately, fetal demise [65]. Therefore, early diagnosis and intervention before hemorrhagic shock lower the fetal mortality rate. Until 1958, fetal mortality was 59% [5]. Others claim fetal mortality of 70% for all-cause spleen rupture [6, 50]. In the English literature, between 1958 and 2011, the fetal mortality rate with a spontaneous splenic rupture in pregnancy was 42.9% and is declining [42]. The fetus has survived after two emergent laparoscopic splenectomies [61, 62]. In all cases of percutaneous angioembolization, pregnancy continued to  $\geq 35$  weeks [12, 58, 64].

Although rare (1.3% of ectopic pregnancies), an ovum could implant within the peritoneal cavity (abdominal pregnancies) either directly (primary abdominal pregnancies—extremely rare) or because of tubal rupture (secondary abdominal pregnancies). William E. Studdiford described the criteria for *primary abdominal pregnancy* in 1942 [66] as follows:

- Normal fallopian tubes and ovaries,
- No evidence of uteroplacental fistula,
- Pregnancy is related exclusively to the peritoneal surface and early enough to eliminate the possibility of secondary implantation after primary nidation of the Fallopian tubes.

#### 24.2.2 Incidence

The spleen is one of the rarest sites for abdominal pregnancies, with 32 cases of primary splenic pregnancy reported worldwide, 28 in the English literature until 2021 [67]. The patients’ mean age is 25 years, but the age range is highly variable (19–41 years) [68–71].

## 24.2 Primary Splenic Pregnancy

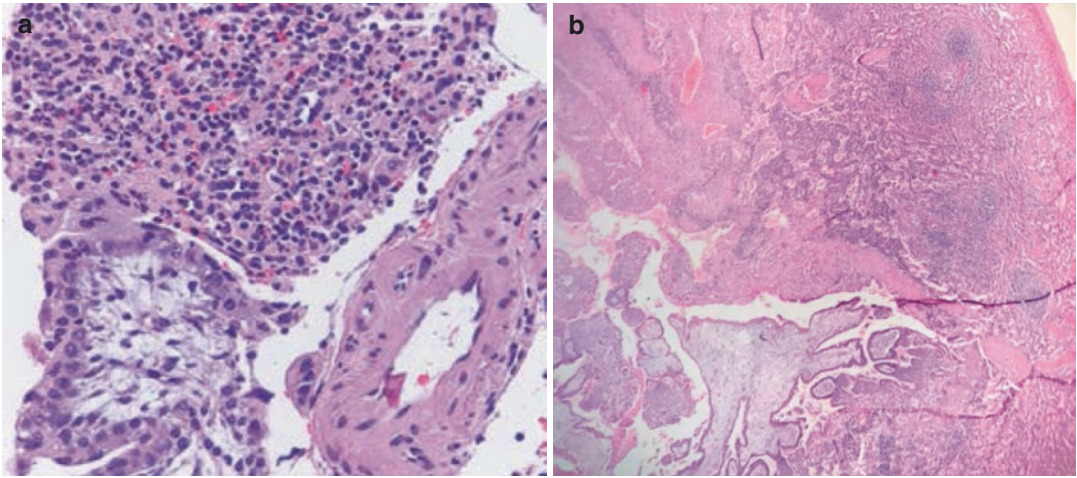
### 24.2.1 Definition and Classification

In approximately 2% of pregnancies, the implantation site is not the uterine cavity (ectopic pregnancies): The most common site of ectopic implantation is the Fallopian tube (95.5%).

### 24.2.3 Risk Factors and Pathophysiology

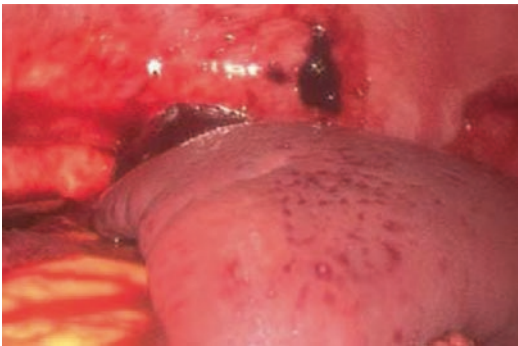
Risk factors for any location ectopic pregnancy are similar and listed in Table 9.1. The intrauter-





**Fig. 24.6** (a) Histopathological examination (H&E;  $\times 20$ ): chorionic villi within the splenic tissue. (Reproduced with permission from [68]). (b) Products of conception

are subcapsular in location and surrounded by the lymphoid follicles of the spleen (H&E;  $\times 100$ ). (Reproduced with permission from [71] under the CC BY 4.0)



**Fig. 24.7** Laparoscopic view, a hemorrhagic lesion at the superior splenic pole. (Reproduced with permission from [68])

ine device (IUD) was present in 14–25% of patients [67, 71, 72], while 8% of early abdominal ectopic pregnancies occurred with an IUD in place [73].

The liver and the spleen are more favorable for implantation because they are flat organs, rich in blood flow, and easily reached by the fertilized ovum (Fig. 24.6) [74]. However, both cannot allow placental attachment, thus leading to rupture with massive hemoperitoneum (Fig. 24.7) [75]. Therefore, splenic pregnancy presents earlier than other abdominal ectopic pregnancies, mainly presenting with acute abdomen and hemoperitoneum. The splenic parenchyma can-

not distend, and most ruptures with bleeding occur up to 8 weeks' gestation [67, 72], although there are cases of bleeding at 10–14 weeks of pregnancy. Due to splenic bleeding in early pregnancy, most gestational sacs are 2–3.5 cm in diameter [71]. No single predilection site exists on the spleen for implantation [67]. The gestational sac can be in the upper and lower poles and hilum [71].

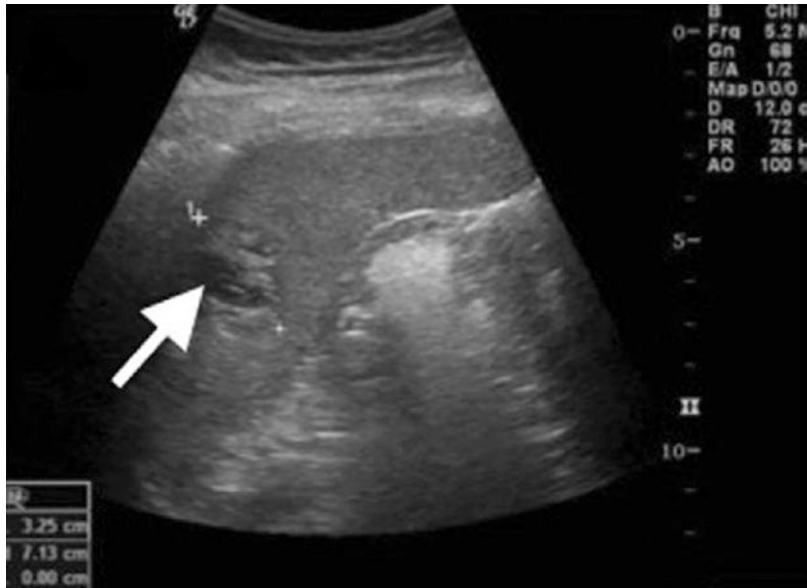
#### 24.2.4 Clinical Presentation

A young female of reproductive age presenting with amenorrhea, abdominal pain, and shock is predominantly considered a ruptured ectopic pregnancy of any location. Approximately 73% of splenic pregnancies have an emergent presentation [67].

A typical presentation is sudden or short-lasting abdominal pain radiating to the left shoulder (*Kehr's sign*). Abdominal pain can be localized or diffuse depending on the severity of intraperitoneal bleeding. With massive bleeding, hemodynamic shock develops with pallor and cold sweat, increased pulse, and systolic blood pressure  $<100$  mmHg [67]. Nonemergent presentation is a woman with amenorrhea complaining of left upper quadrant pain [74, 76].



**Fig. 24.8** Abdominal ultrasound shows the mass at the superior aspect of the spleen. (Reproduced with permission from [72])



### 24.2.5 Differential Diagnosis

Nearly all patients with ruptured splenic pregnancy have a preoperative diagnosis of ruptured ectopic pregnancy from elevated  $\beta$ HCG, hemoperitoneum, and amenorrhea [67]. Other causes/locations of hemoperitoneum should be searched for depending on the medical history or history of abdominal trauma.

### 24.2.6 Diagnosis

#### 24.2.6.1 Laboratory Findings

For patients with abdominal pain and signs of hypovolemic/hemorrhagic shock, a complete blood count, BUN, creatinine, liver, and pancreatic enzymes are mandatory. With amenorrhea,  $\beta$ HCG should be checked.

#### 24.2.6.2 Transvaginal Ultrasound

Elevated  $\beta$ HCG indicates the transvaginal US to define the uterus and gestational status. Ectopic pregnancy should be excluded from a normal-sized uterus with a thickened endometrium without an individual gestational sac.

#### 24.2.6.3 Transabdominal Ultrasound

If fallopian tube ectopic pregnancy is excluded, the transabdominal US should check other

potential locations of ectopic pregnancy. Most splenic gestations were subcapsular with an irregular mass exceeding the splenic contour (Fig. 24.8). An irregular mass outside the contour of the spleen should raise the suspicion of splenic pregnancy [77]. A few cases of splenic pregnancy have been diagnosed by the US alone. These patients were hemodynamically stable, with most presentations before splenic rupture [67].

#### 24.2.6.4 Abdominal CT

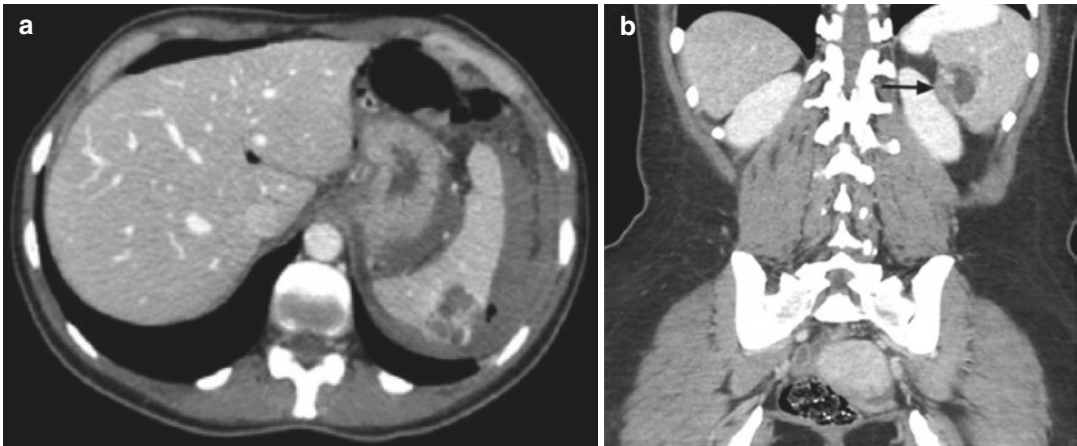
If the transabdominal US is unequivocal in hemodynamically stable patients, contrast-enhanced abdominal CT is indicated (Fig. 24.9). Abdominal CT has been used in 32% with an accuracy of 100% [67].

#### 24.2.6.5 Abdominal MRI

When pregnancy is suspected, MRI reveals the location and size of the gestation sac [72].

### 24.2.7 Treatment

Although splenectomy is often performed, splenic preservation should be encouraged to treat ruptured splenic pregnancies. In general, treatment options for ectopic pregnancy are based on  $\beta$ HCG levels.



**Fig. 24.9** (a) Axial abdominal CT shows heterogeneous hypervascular mass at the superior splenic pole. (Reproduced with permission from [68]). The intraoperative view is in Fig. 24.7). (b) Coronal abdominal CT

shows a  $4.5 \times 3.5$  cm round lesion containing fluid with heterogeneous enhancement on the posterior pole of the spleen. (Reproduced with permission from [78])

Medical management, consisting of systemic or local injection of methotrexate (MTX), is recommended for asymptomatic patients with a  $\beta$ HCG  $<5000$  IU/L [79].

Procedures (from minimally to maximally invasive) for the treatment of splenic pregnancy are [67] as follows:

- Im. MTX injection,
- Intra gestational sac feticide injections,
- Splenic artery embolization plus im. MTX injection,
- Splenic preservation techniques,
- Splenectomy.

Splenectomy was the only treatment up to 2010 [67]. Since 2010 splenic preservation methods have been increasingly used.

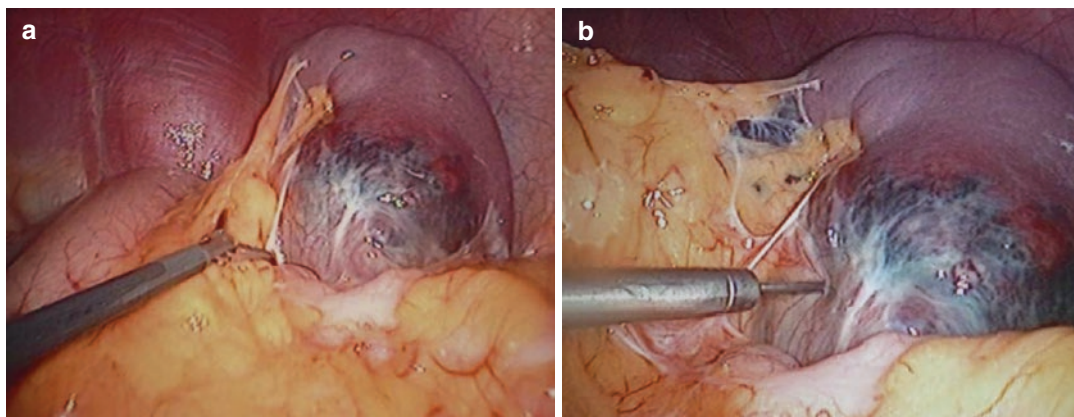
#### 24.2.7.1 Intramuscular Methotrexate Injection

Im. MTX injection (1 mg/kg) is recommended for early ectopic pregnancies ( $\beta$ HCG  $<5000$  IU/L) in stable patients. If the treatment is unsuccessful (rising  $\beta$ HCG levels or enlarging gestational sac), more invasive methods are used (see further text).

#### 24.2.7.2 Intra gestational Sac Feticide Injections

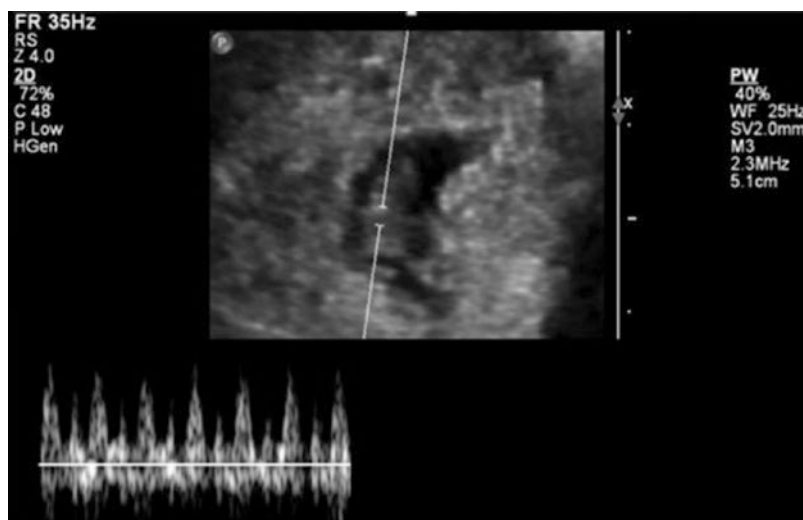
For the intra gestational sac feticide instillation principle, there are two types of intralesional solutions and two types of access to the ectopic gestational sac. Feticide solutions include MTX and potassium chloride (KCl), both proven very efficient even with  $\beta$ HCG  $>5000$  IU/L [78]. KCL's success rate for ectopic pregnancy in any location is 99.5% [80]. The dose of MTX is 1 mL (50 mg/m<sup>2</sup>), while KCl is 2 mL [78, 79]. Caution is warranted with gestational sac KCL administration. Side effects are extremely rare with 2 mL KCl concentrations [80]. Risks associated with KCl-induced fetal demise include unintentional injection into the maternal circulation, potentially resulting in maternal cardiac rhythm abnormalities or maternal cardiac arrest [81]. Continuous maternal cardiac tracing is recommended throughout the procedure in a center capable of managing adverse cardiac outcomes [78].

The route of feticide solution delivery is percutaneous and surgical. Percutaneous instillations are done under CT or US control. In contrast, surgical instillation is minimally invasive using laparoscopy (Fig. 24.10). Postprocedural transabdominal US confirms



**Fig. 24.10** (a) Laparoscopic adhesiolysis around splenic pregnancy. (b) Injection of methotrexate into the gestational sac. (Reproduced with permission from [79])

**Fig. 24.11** Transabdominal ultrasound shows persistent fetal pulse following systemic and local methotrexate treatment and before intralesional potassium chloride administration. (Reproduced with permission from [78])



fetal demise without a fetal pulse. Postprocedural fetal heart rate is a sign of failed procedure (Fig. 24.11).

### 24.2.7.3 Embolization

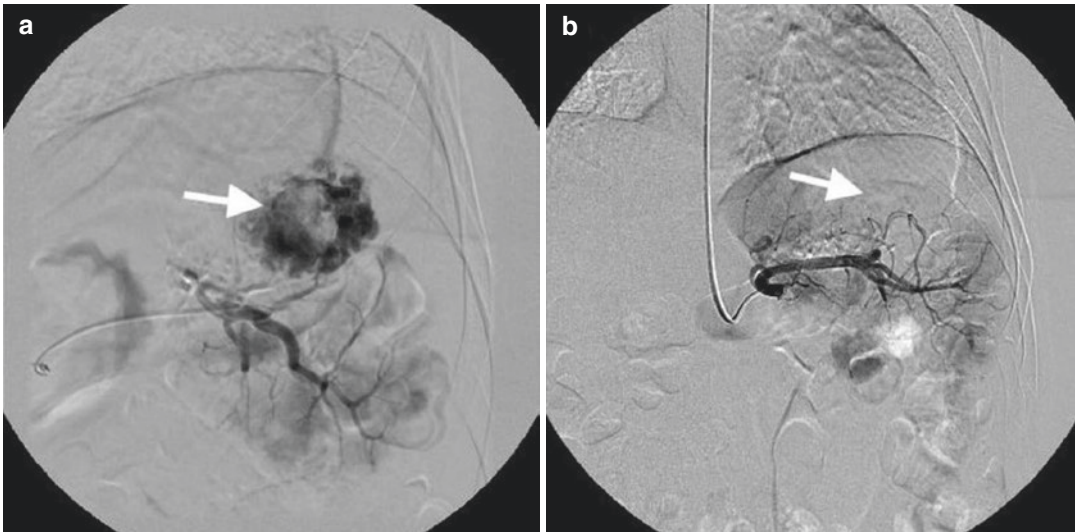
Digital subtraction angiography is performed through percutaneous brachial access. Angiography reveals the pathologic neovascularity of the gestational sac (Fig. 24.12a). The feeding branches are supraselectively catheterized with a microcatheter, and embolization is performed with microspheres. Immediate post-embolization angiography should be performed to evaluate the success of the procedure. It should show the abolishment of the entire pathologic

vascularity (Fig. 24.12b). Adjuvant treatment consists of a single im. dose of MTX 50 mg/m<sup>2</sup>. After 10–14 days, transabdominal US confirms infarct formation and reduction of the avascular cystic splenic lesion (Fig. 24.13).

### 24.2.7.4 Surgical Treatment

#### Laparoscopic Procedures

An accurate preoperative diagnosis is difficult; therefore, laparoscopy should be performed for the diagnosis and treatment. For early splenic pregnancy, even with hemoperitoneum, laparoscopic treatment is optimal in hemodynamically stable patients [68, 77]. Purplish-blue sac-like



**Fig. 24.12** (a) Digital subtraction angiography shows the pathologic neovascularity of the gestational sac (arrow). (b) After selective catheterization and embolization of the feeding branches, immediate postembolization

angiography shows the abolishment of the entire pathologic vascularity (arrow). (Reproduced with permission from [72])

**Fig. 24.13** 10–14 days after the splenic pregnancy embolization, transabdominal ultrasound shows altered echogenicity of the spleen's upper aspect due to early infarct formation and reduction of the cystic splenic lesion, which appears avascular (arrows). (Reproduced with permission from [72])



nodule confirms splenic pregnancy. The diagnosis is more confident with bleeding nodules (Fig. 24.14).

There are no recommendations for the type of procedure. The most minimally invasive procedure is MTX instillation into the gestational sac (see Sect. 24.2.7.2). When resectional procedures are necessary, partial splenectomy or wedge resection,

including ectopic pregnancy, should be tried. Essential steps are atraumatic mobilization of the spleen, temporary splenic artery occlusion avoiding injury to pancreatic parenchyma, topical hemostatic agents, and absorbable meshes if needed [67]. Also, only a gestational sac can be excised with a bipolar or ultrasonic instrument to lessen the bleeding [76]. The last option is splenectomy.



Despite the method used for the treatment, the entire abdominal cavity should be explored, especially the uterus and adnexa, to check if this process started as a second ectopic pregnancy [79]. This is especially important for IVF-ET patients with a higher rate of heterotopic pregnancies [74].

### Open Procedures

Large hemoperitoneum is better explored in hemodynamically unstable patients through median laparotomy. CS is usually indicated for fetal distress. The performance of splenectomy or splenic preservation procedures depends upon the following:

- The degree of bleeding,
- The status of the spleen,
- Penetration of the gestational sac into the spleen.

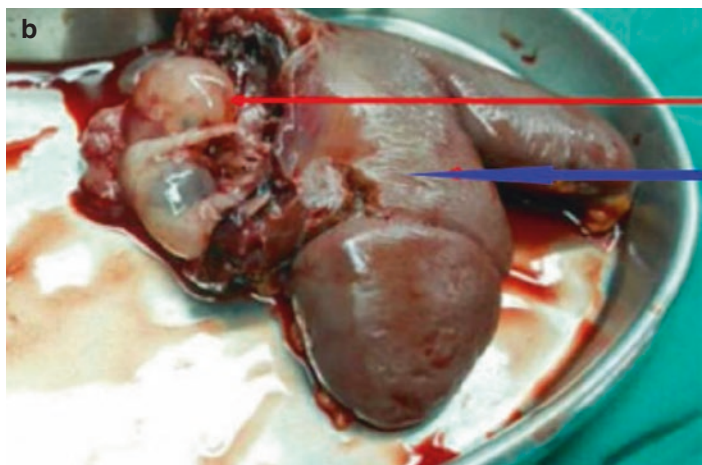
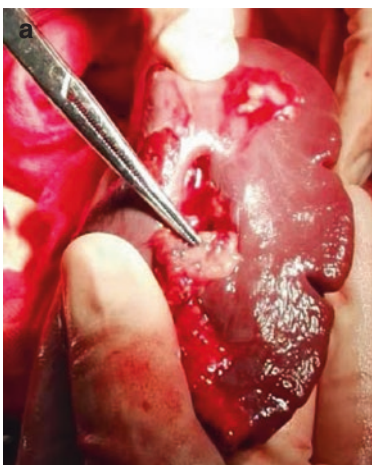
Intraoperative confirmation of early splenic pregnancy is a zygote with chorionic villi (Fig. 24.15a) or fetus on the surface of the spleen in more advanced pregnancy (Fig. 24.15b).

### 24.2.7.5 Anesthetic and Perioperative Management

See Chap. 2. Spleen preservation avoids overwhelming post-splenectomy infection syndrome, a frequently life-threatening condition [84]. Also, splenectomized patients are immunocompromised to primary cytomegalovirus (CMV) infection [85]. With future pregnancies, there may be an increased risk of congenital CMV infection. After splenic embolization or partial or total splenectomies, vaccination for *S. pneumonia*, *H. influenzae*, and *N. meningitidis* is indicated [72]. After local feticide injections or splenic surgical procedures,  $\beta$ HCG drops to zero; after splenectomy, from 7 to 14 days, depending on the values at presentation (Fig. 24.16). After intralesional feticide administration, the decline is slower, from 1 to 2 months [78, 79].



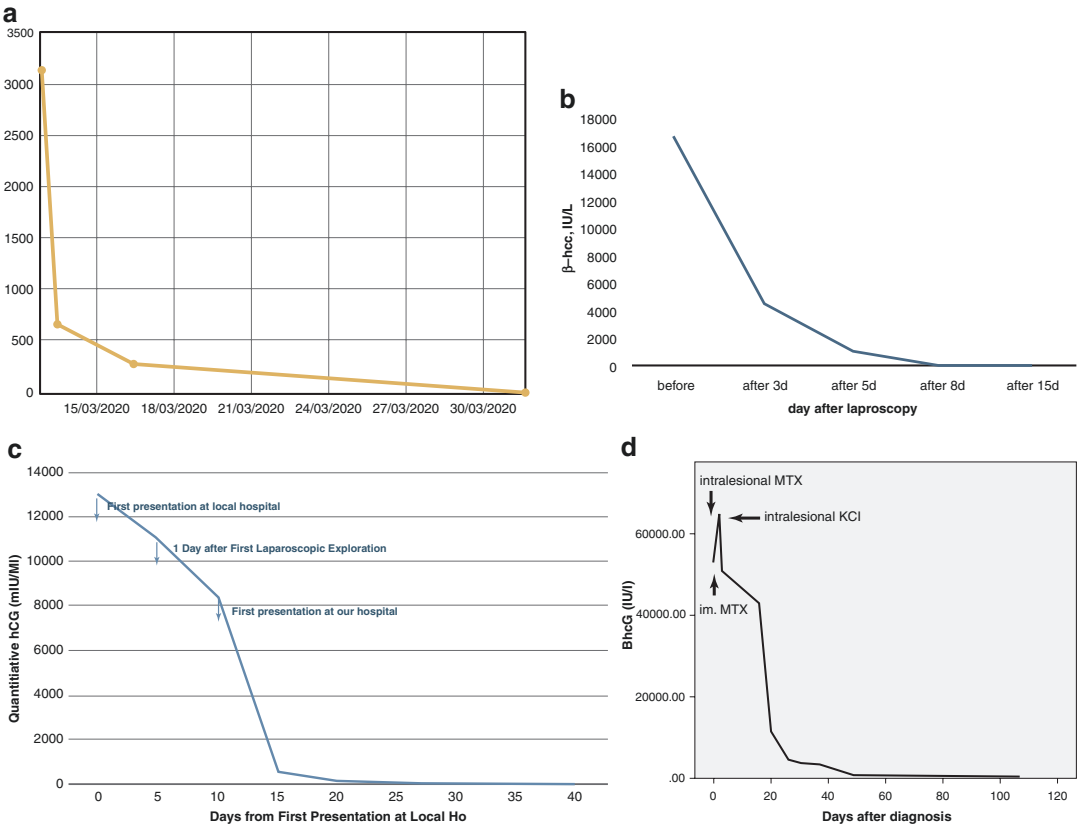
**Fig. 24.14** Laparoscopic detection of a purple-blue sac-like nodule (3 cm in diameter) in the dorsal pole of the spleen. (Reproduced with permission from [82])



**Fig. 24.15** (a) Spleen 6 × 10 cm after splenectomy and zygote with chorionic villi (tip of the instrument). (Reproduced with permission from [69]). (b) Spleen

10 × 5 cm after splenectomy (blue arrow) and the fetus (red arrow) 3.5 × 4.0 cm (amenorrhea of 56 days) on the splenic surface. (Reproduced with permission from [83])





**Fig. 24.16** (a–c) Decrease in serum b-human chorionic gonadotropin ( $\beta$ HCG) concentration days after splenectomy. (Reproduced with permission from [67, 76, 82]). (d) Declining  $\beta$ HCG trend following KCl administration

on day 5 post-admission (MTX administrations without effect).  $\beta$ HCG b-human chorionic gonadotropin, MTX methotrexate. (Reproduced with permission from [78])

The operative specimen sent to the pathohistological examination reveals gestational villi in the spleen mass. With splenic preservation methods, serum  $\beta$ HCG and the transabdominal US confirm a lack of splenic pregnancy after a month.

#### 24.2.7.6 Prevention and Treatment of Preterm Labor

See Chap. 4.

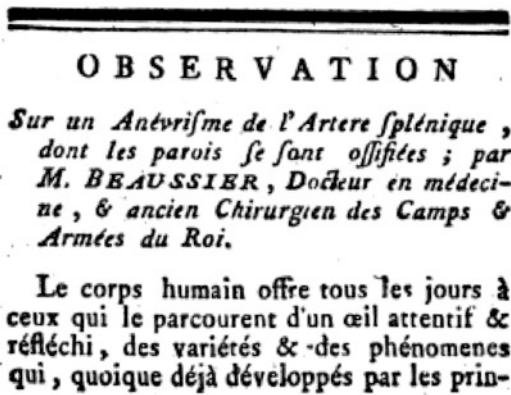
#### 24.2.8 Prognosis

Despite being a life-threatening condition, no mortality has been reported [67]. This may be related to misdiagnosis as a spontaneous splenic rupture and publication bias in not reporting fatal outcomes.

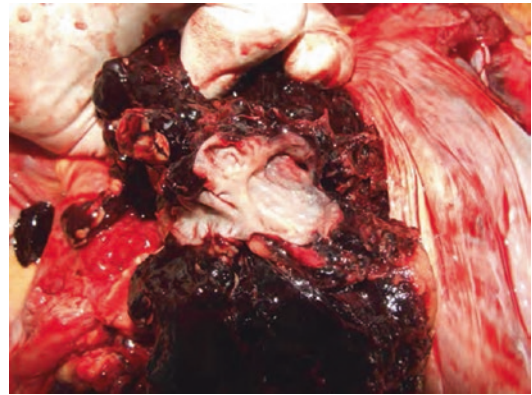
### 24.3 Spontaneous Splenic Artery (Aneurysm) Rupture

#### 24.3.1 Historical Perspective

A splenic artery aneurysm (SAA) is an abnormal dilation of more than 1 cm in diameter of the splenic artery. The first case of SAA was published in 1770 by Beaussier [86] during the anatomic dissection of a 60-year-old female cadaver, which he performed 10 years before publishing it (Fig. 24.17). This and the second case reported by Parker in 1844 [87, 88] were omitted from the literature. Priority was mistakenly given to Crisp in 1847 by all subsequent authors, possibly because he had also erroneously credited Parker with describing the first case [89]. Winkler, in 1903, first identified SAA in a living person (a



**Fig. 24.17** Original part of the text on the first case of splenic artery aneurysm in the nonpregnant female by Beaussier. The text was published in 1770 in the *Journal de Medecine, Chirurgie, Pharmacie* [86]



**Fig. 24.18** Ruptured saccular splenic artery aneurysm (2.5 cm in diameter) at the autopsy of a pregnant woman [102]

nurse) during laparotomy for abdominal pain of 8-year duration [90].

An association with pregnancy started with Corson's first description of the sudden and unexpected death of a 29-year-old multigravida at 8 months' gestation. The diagnosis of SAA rupture was made on postmortem examination in 1869 [91]. Sheehan and Falkiner, in 1948, noted that 56% of females who had an SAA rupture were pregnant and in their last trimester [40].

## 24.3.2 Incidence

### 24.3.2.1 General Population

SAA is the most common (60%) of all visceral artery aneurysms. More than 50% of aneurysm ruptures in women under 40 are related to pregnancy. The arteries most often involved are, in declining order, the aorta, cerebral arteries, splenic arteries, renal arteries, coronary arteries, and ovarian arteries [92]. The incidence of SAA is unknown because of the following: (1) A vast majority of SAAs are smaller than 2 cm, (2) they remain asymptomatic, (3) they are generally encountered as autopsy findings, [56] and (4) due to destruction of spleen parenchyma and smaller vessels by hematoma, and some are classified as spontaneous spleen ruptures. Until 1953, there were 204 recorded ruptured and unruptured SAA [93, 94]. The SAA incidence in autopsy series

reports ranges from 0.01 to 10.4% [95, 96]. Likely, the figures quoted in most autopsy series are underestimated as the SAA can be difficult to identify unless specifically sought, and autopsy studies have different age ranges included in the analysis. SAAs are being detected incidentally with modern imaging for unrelated conditions. SAA is at least twice as common in women [97], while other types of aneurysms are five times as frequent in males [98].

The majority of SAAs are <3 cm in diameter and are usually saccular, isolated, and located in the mid or distal portion of the splenic artery, frequently at an arterial bifurcation [99–101]. Macroscopically, two principal types of SAA are saccular and fusiform (Fig. 24.18).

### 24.3.2.2 Splenic Artery Aneurysm Rupture

The complication of an SAA is a rupture with a risk of 3–9.6% [100, 103]. More than 400 cases of ruptured SAAs in the general population have been reported, with approximately 20–50% during pregnancy [56, 94, 100, 103–111]. A summary of 58 recorded cases was made by Anderson and Gray in 1929, adding their case [112], and Machemer and Fuge in 1939 collected a further 24 cases and added one of their own [113]. Sherlock and Learmonth in 1942 [114] stated that SAA sometimes declares itself during pregnancy, which may partly account for the larger

number of females in the general population. SAAs are the most frequent in the general population, with an incidence of around 60%. Among visceral aneurysms, the SAA is the most common (95%) in young pregnant women, and a greater number of diagnoses are made during pregnancy, often due to aneurysmal rupture. Of all SAAs, 65% are present in pregnancy, and 50% rupture during pregnancy [115]. Grand multiparous form about 40% of women with SAAs [116]. In a 10-year review of maternal mortality in Singapore, no case of SAA was identified [117].

### 24.3.2.3 Trimester Distribution

SAA has been increasingly diagnosed in pregnancy, mainly due to increased US and high-resolution cross-sectional imaging techniques used [101]. Sheehan and Falkiner, in 1948, noted that 56% of females who suffered a rupture of an SAA were pregnant and in the last trimester [40]. The distribution of SAA rupture during pregnancy is [100, 118–122] as follows:

|                            |      |
|----------------------------|------|
| First to second trimesters | 12%, |
| Third trimester            | 69%, |
| Childbirth                 | 13%, |
| Puerperium                 | 6%.  |

### 24.3.3 Risk Factors

There are two distinct types of splenic artery rupture. One is a spontaneous splenic rupture where no underlying pathology of the splenic artery can be found, and another is a spontaneous rupture of the SAA. True SAA (in the general population) is most commonly associated with pregnancy and portal hypertension [123–127]. Other conditions include essential hypertension, angiodysplasia, atherosclerosis, diabetes, intracranial aneurysm, polyarteritis nodosa, alpha-1-antitrypsin deficiency, and infective factors [111, 125, 128, 129].

SAA rupture rates in the general population are 2–3% [95, 121]. The SAA size is usually >2.5 cm at rupture [103]. However, rupture of smaller aneurysms has been reported [103, 119, 121]. Since 2000, multiparas 54.8% [130].

#### 24.3.3.1 Spontaneous Splenic Artery/Vein Rupture

Cases of spontaneous rupture of the normal splenic artery (or vein) occurred with long-standing liver cirrhosis with portal hypertension [131]. Prolonged hypertension may be contributory [132, 133].

#### 24.3.3.2 Spontaneous Splenic Artery Aneurysm Rupture

Most ruptured SAAs in pregnancy have occurred during the third trimester [111]. Therefore, increasing gestation gradually increases the risk of SAA rupture. Apart from advanced pregnancy, other risk factors include portal hypertension [134–136], atherosclerosis, congenital abnormalities of the vessels, inherited vascular and connective tissue disorders (medial fibrodysplasia), vascular trauma, inflammatory processes, and degenerative arterial disease [45, 100, 124]. Although the average parity of women at rupture is 4.5 [95, 101, 111, 121, 125], there are cases with nulliparous women [127, 134, 137]. High blood pressure, common in preeclampsia–eclampsia, is a precipitating factor for SAA rupture, especially during labor [138].

### 24.3.4 Pathophysiology

The mechanisms involved in the formation of this vascular defect remain unclear. Most theories consider hemodynamic and hormonal alterations in the late stages of pregnancy [139]. Although the risk of rupture mainly exists in the third trimester of pregnancy (see Sect. 24.3.3.2), there are cases of SAA rupture during the first trimester of pregnancy [140–143]. Only 5% are found during puerperium [105].

One of the mechanisms promoting the vascular defect in splenic arteries during the late stages of pregnancy seems to be the escalating increase of the circulating estrogens and progesterone during pregnancy [125]. The elevation of the levels of these hormones has been associated with the promotion of various structural alterations in the arteries, such as the disruption of the internal elastic lamina, fragmentation of elastic fibers, degeneration of smooth muscle fibers, and failure

of elastin formation [144]. Additionally, the elevated levels of relaxin throughout the third trimester of pregnancy may affect the elasticity of the splenic artery wall [145] and could probably weaken the arterial wall [101, 118, 146]. Especially in the case of multiparity, repeated exposure to these hormonal shifting could explain the increased incidence of rupture of SAA in this group of pregnant women.

Also, the hemodynamic changes during the late stages of pregnancy are implicated in the etiology of SAA ruptures. The enlarged uterus compresses the aorta and the iliac arteries, resulting in higher flow in the splenic artery, increasing the likelihood of SAA development and progression. Moreover, the increases in blood volume and cardiac output, along with the relative portal congestion, contribute to forming SAAs [139]. Also, compression of other surrounding pathologic conditions contributes to faster development and progression of SAA or causes rupture of the normal splenic artery [104]. The vessel wall is in a continual state of self-maintenance and self-regulation, including remodeling in response to hemodynamic stress [106]. Remodeling of the vessel wall causes similar histological lesions, regardless of the pathogenic factors [147].

### 24.3.5 Clinical Presentation

Apart from asymptomatic SAA found incidentally during pregnancy, two types of presentations include symptomatic or ruptured SAA.

#### 24.3.5.1 Ruptured Splenic Artery Aneurysm

The rupture can be sudden or two-stage, present in 20–25% [119–121]. In the early stages of rupture, diffuse tenderness in the upper abdomen, left hypochondrium, or over the uterine fundus may be elicited. With prolonged bleeding, derangement of the vital signs indicates hemodynamic shock. A developing retroperitoneal hematoma may produce severe nausea and vomiting. A palpable mass in the left hypochondrium may be present.

The physical course either can consist of one stage, leading to dramatic collapse as a result of the inability of self-containment of bleeding, or can present in a two-stage sequence, first described by Bockerman in 1930, when initial tamponade of bleeding in the lesser sac was made by clots blocking the foramen of Winslow [145, 148]. Initial hemorrhage into the lesser sac may cause pain and transient hypotension; the gradual increase of pressure in the lesser sac would be suddenly followed by a rupture into the greater sac and lead to massive intraperitoneal bleeding and shock, causing the patient to collapse. The initial phase, where bleeding remains confined to the lesser sac, provides vital time for diagnosis and preparation for intervention [101, 118, 119, 146]. The “sentinel” period between the initial and subsequent hemorrhages may take 6–96 h, although longer sentinel periods were described [120]. This phenomenon of “double rupture” was previously reported in 25% [127, 149] and since 2000 in 14.7% [130]. When ruptured, it usually causes acute left-sided abdominal pain that may radiate to the back, flank, and subscapular region and may cause shock, abdominal distension, and death. Due to diaphragmatic irritation with blood and abdominal pain, patients can also present with chest pain and dyspnea [132]. Pregnant women tend to be younger and have fewer adhesions from previous surgery than the general population; therefore, rupture occurs almost exclusively in the free peritoneal cavity [124, 125, 150].

#### 24.3.5.2 Symptomatic Splenic Artery Aneurysm

The symptoms of an unruptured aneurysm are variable. According to Pasternack and Shaw [151], colicky pain in the left epigastrium or hypochondrium may occur. Exertion or changes of posture characteristically increase it. There may also be stomach, gallbladder, or colon symptoms. A periumbilical pulsating mass may be felt, or a systolic bruit heard. Physical signs do not reliably indicate an SAA [101].

### 24.3.6 Differential Diagnosis

Ectopic pregnancy is one of the first differential diagnoses for cases presented during the first trimester of pregnancy [140–143]. Approximately 70% of cases are diagnosed initially as uterine rupture [92]. Differential diagnosis includes pancreatic cysts or pseudocysts, which are more frequent with a history of pancreatitis. Presentation similar to a massive pulmonary embolism characterized by left-sided chest pain, breathlessness, and low oxygen saturation has been reported [152].

### 24.3.7 Diagnosis

The key to effective management of a ruptured SAA is clinical suspicion, combined with the accurate implementation of diagnostic imaging, particularly abdominal US and angiography, if the hemodynamic stability permits. Since 2000, preoperative imaging was made in 70.7% [130].

A diagnosis of ruptured SAA should be considered in (1) a pregnant woman who complains of the sudden onset of severe left upper abdominal pain regardless of whether pain or shock is prominent at the time of evaluation and (2) when a hemorrhagic shock in a pregnant woman without obstetric bleeding is present [134, 153].

Höglér, in 1920, made the first preoperative diagnosis based on a bruit and a pulsatile mass on fluoroscopy [154]. Another case of one of the first preoperative diagnoses in the general population based on X-ray examination alone was made by Lindboe in 1932 [155]. In 1950, Evans obtained the first translumbar aortogram, demonstrating a successful SAA operation. Baum, in 1965, used selective angiography in making a preoperative diagnosis.

Screening of the splenic artery by transabdominal US and Doppler (Fig. 24.19) should be considered selectively in pregnant patients with

predisposing factors like hypertension, multiparity, and liver and pancreatic diseases. However, its utility is limited by operator dependency, obese patients, bowel gas shadow, and arteriosclerosis [156]. Gray-scale US is not a useful diagnostic tool for SAA. Clinicians should use the color Doppler US to evaluate the splenic hilum [156]. The likelihood of missing smaller lesions is also quite high because of limited spatial resolution [157].

Although it is not the first-line investigative tool for SAA, a plain abdominal X-ray for some other abdominal pathology may reveal calcified SAA as a characteristic calcified ring with a central lucent area to the left of the first lumbar vertebral body [139].

Contrast-enhanced abdominal CT defines the abdominal aorta with its branches. A splenic artery with SAA can be delineated (Fig. 24.20). The CT should be carefully analyzed because there are cases with more than one SAA [107, 159]. 3D reconstruction is important to precisely define the SAA's location and diameter, essential parameters for preoperative planning (Fig. 24.21).

Magnetic resonance angiography of the abdominal aorta and branches is performed in the general population. MR angiography accurately defines the abdominal aorta with its branches and can accurately define SAA. There are no cases of MR-proven SAA in pregnancy.

### 24.3.8 Treatment

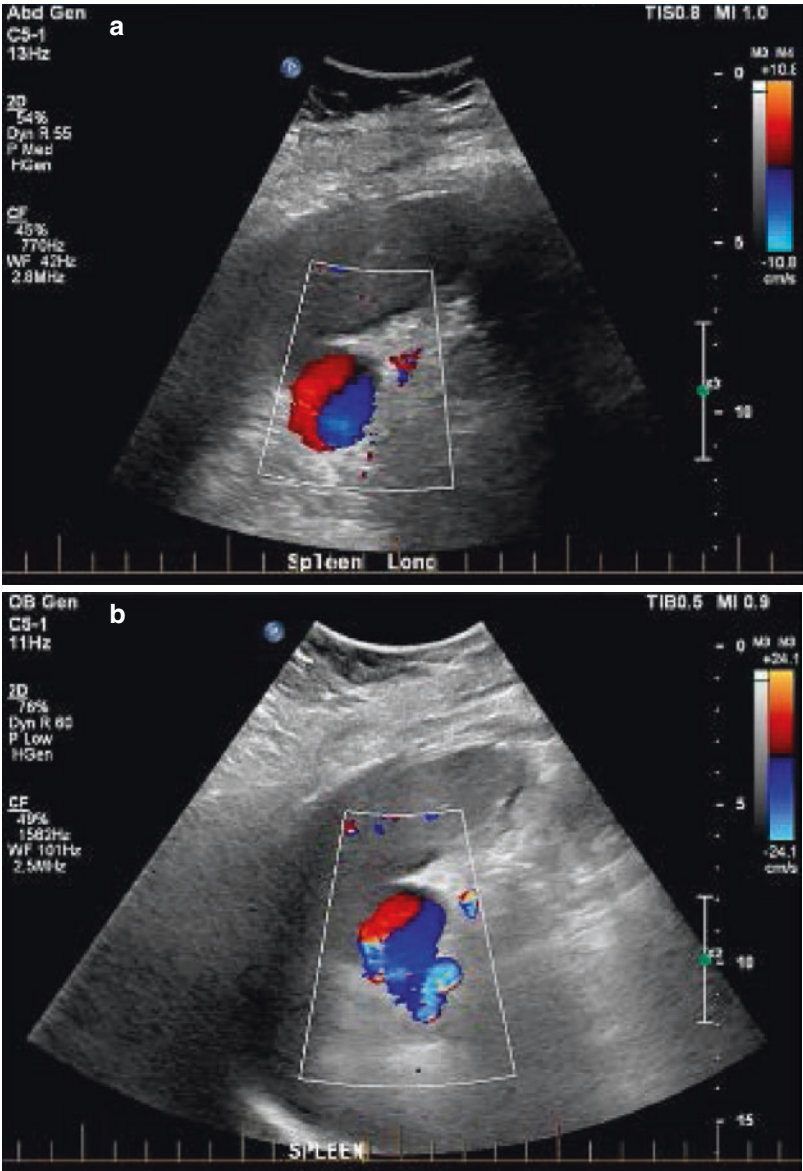
#### 24.3.8.1 Ruptured SAA

Concerning intervention options, apart from the need for initial aggressive resuscitation, embolization of the SAA or emergency surgery is the main treatment option [139, 145].

The first successfully treated case in pregnancy was described in 1940. Aneurysmectomy with splenectomy or distal pancreatectomy with splenectomy with ligation of the proximal and distal splenic artery, or aneurysmectomy with splenic conservation, has been used [92, 118]. Since 2000 ruptured SAA have been primarily managed by laparotomy (81.3%), typically with splenectomy [130].

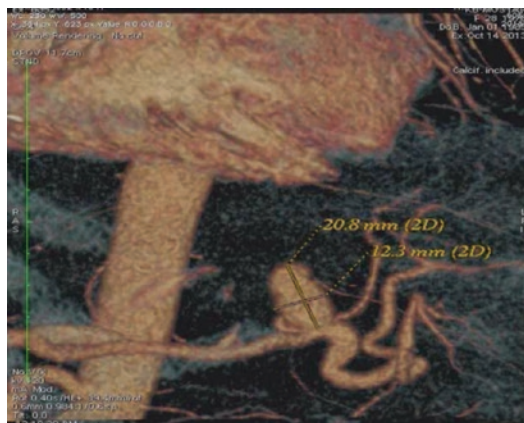


**Fig. 24.19** (a) Color Doppler ultrasound shows the characteristic “yin-yang” appearance of turbulence within the splenic artery aneurysm. (b) Ultrasound image of splenic hilum demonstrating splenic artery aneurysm with turbulent color Doppler flow [158]



**Fig. 24.20** Abdominal CT angiography shows a splenic artery aneurysm arising from the mid-splenic artery and another smaller aneurysm at the proximal splenic artery. The perisplenic and retroperitoneal hematoma was evacuated during the operation the previous day. (Reproduced with permission from [107] under the CC BY 3.0)





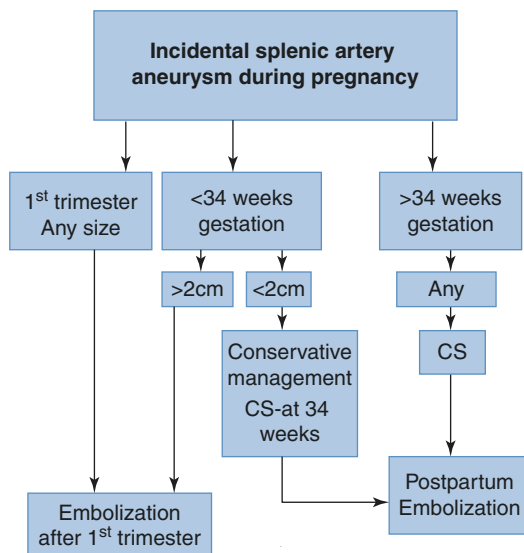
**Fig. 24.21** Abdominal CT angiography with 3D reconstruction verifies the exact position of saccular splenic artery aneurysm measuring 20.8 × 12.3 mm. (Reproduced with permission from [160])

Splenic conservation is desirable but is difficult in the emergency setting with ruptured SAA [118, 161]. Angiography and embolization have been described for pseudoaneurysms and unruptured true aneurysms [118]. In high-risk patients, arterial embolization using coils can be an effective early treatment [92, 101, 146]. There are cases when emergency CS is performed with pre-operative suspicion of placental abruption or uterine rupture. If the general or abdominal surgeon is unavailable, some patients are sent for a contrast-enhanced abdominal CT postoperatively [107] due to the following: (1) continuous bleeding and (2) no ionizing radiation to the fetus [107]. This is not recommended diagnostic and treatment algorithm. The bleeding should be stopped during the initial operation.

#### 24.3.8.2 (A)Symptomatic SAA

The management of an unruptured SAA is presented in Fig. 24.22.

Elective resection or stenting in pregnant women and women of childbearing age is recommended for SAA >2 cm [111, 121, 124].



**Fig. 24.22** Management of splenic artery aneurysm detected during pregnancy. CS Cesarean section [162]

Surgical options include aneurysmal resection, with or without splenectomy, via laparotomy or laparoscopy. Aneurysms located in the proximal or middle third of the splenic artery may be treated by simple excision with proximal and distal splenic artery ligation. The method preserves the spleen, vascularized by the short gastric vessels. Aneurysms in the distal third are resected with splenectomy.

Endovascular techniques include transcatheter embolization and percutaneous angiographic embolization [130], mostly used in the puerperium. *Postembolization syndrome* and infarcts are common events (30%) but generally resolve without a sequel. The gestational age is an important parameter for the indication of this technique in pregnancy.

### 24.3.9 Prognosis

#### 24.3.9.1 Maternal Outcome

There are some 400 reports in the general population with an overall mortality rate of 25% [124]. Approximately 25% involve pregnant women,

with disproportionately higher mortality. Ruptured SAA during the 1940s and 1950s resulted in maternal mortality of 93.3% [163, 164]. Until 1977, maternal mortality declined to 70% [120]. In Australia, in 30 years (1967–1999), only four maternal deaths occurred due to SAA rupture [164]. For comparison, in the UK, from 1988 to 2002, there were seven definite (and one possible) ruptured SAAs [124]. Since 2000, there has been no maternal mortality in unruptured SAA, but 25.7% in SAA rupture [130].

In early pregnancy, when clinicians do not expect SAA rupture, maternal mortality is high due to cardiac arrest during the early postoperative period [140, 141].

#### 24.3.9.2 Fetal Outcome

Due to mostly massive bleeding and early development of maternal hemodynamic instability, the fetal mortality rate until 1977 was 95% [120]. Since 2000, there has been no fetal mortality in unruptured SAA but 50% in SAA rupture [130].

## 24.4 Spontaneous Splenic Vein (Aneurysm) Rupture

### 24.4.1 Historical Perspective and Incidence

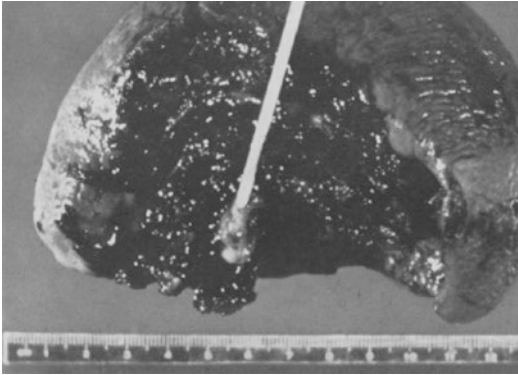
Portal system aneurysms can be divided into two types as follows: extrahepatic and intrahepatic. A splenic vein aneurysm (SVA) is a true aneurysm and belongs to the extrahepatic category. In 1953, Lowenthal and Jacob [165] described the first case of SVA in the general population, and 10 pregnant women with splenic vein rupture were described [133, 166–174]. Rahn and Steffen described splenic vein rupture in a pregnant woman in 1959 [168]. Up to 1961, there were only two references of *spontaneous* splenic vein rupture in the general population [131, 175] and two cases of spontaneous rupture in pregnancy [132, 133]. Splenic vein rupture usually occurs during the third trimester, whereas splenic artery rupture has been described from the first trimester to the puerperium. There is only one case of SVA rupture occurring immediately postpartum

[166]. Despite the difference in incidence, SAA and SVA share several etiological factors, presenting symptoms, clinical course, complications, and management.

### 24.4.2 Etiology

The origins of the ruptures due to vascular pathologies at pregnancy may be hormonal, genetic, thrombotic, or mechanical. The etiology of splenic aneurysms is speculative and may include congenital connective and elastic tissue changes [170, 171]. Aneurysms may also be acquired due to trauma, inflammation, portal hypertension [172, 174], or cirrhosis [131, 175].

Splenic aneurysms are more common in multiparous women. Therefore, pregnancy may influence their development because of changes in hemodynamics and increased progesterone levels [95]. The physiological increase in blood volume and cardiac output during pregnancy could lead to portal congestion and splenic arteriovenous shunting and, together with progesterone-induced vasodilation and vessel wall weakness, could favor aneurysm formation. Tolgonay et al. [176] described a case of splenic size increase and SVA due to systemic infection in leukemia patients. After appropriate therapy, a reduction in spleen size was observed, followed by a decrease in splenic vein blood flow and regression of the SVA. Recent studies have shown the alteration of elastic fibers in the internal elastic lamina and fibrodysplasia of the media lamina due to hormonal changes. These factors may become cumulative, explaining the increased rupture rate of the splenic vessels as parity rises [92]. The etiology of SVA in nonpregnant women includes portal hypertension and liver cirrhosis [177], chronic pancreatic inflammation [178], and vessel wall weakness [179]. Splenic vein rupture during pregnancy is associated with acute pancreatic necrosis eroding the splenic vein, acute vessel wall inflammation [133], and SAA rupture into the splenic vein [180]. In other cases, the etiology remains unknown, and splenic vein rupture is labeled “spontaneous” to account for the lack of apparent trauma or disease.



**Fig. 24.23** Hilar surface of the spleen shows hemorrhage about splenic vessels. A probe is inserted into the spontaneous perforation of the splenic vein. (Reproduced with permission from [133])

### 24.4.3 Risk Factors

There are only two cases of pregnant patients with spontaneous rupture of the normal splenic vein. Gross and microscopic examination of the spleen revealed splenomegaly, with the spleen measuring  $11.5 \times 8.5 \times 7$  cm and weighing 252 g (Fig. 24.23). No specific pathologic lesion was seen grossly or microscopically in the spleen. There was a perforation of one of the branches of the splenic vein at the hilum of the spleen without underlying pathology. Prolonged hypertension may be a contributory factor [132, 133].

### 24.4.4 Pathophysiology

#### 24.4.4.1 Cirrhosis

The SVA was associated with portal hypertension and liver cirrhosis in 50% of nonpregnant patients. Three clinical observations could support the pathogenetic mechanism of splenic vein rupture:

1. Splenomegaly in cirrhosis is not only caused by portal congestion, but it is mainly due to tissue hyperplasia and fibrosis. The increase in spleen size is followed by increased splenic blood flow, which participates in portal

hypertension, actively congesting the portal system [181],

2. Increased resistance to portal blood flow is the primary factor in the pathophysiology of portal hypertension and is mainly determined by the morphological changes occurring in chronic liver diseases. The transmission of the increased blood flow and pressure to the splenic vein may lead to progressive dilation and weakness of the vein wall,
3. Portal hypertension in advanced cirrhosis is characterized by increased vasoactive mediators such as prostaglandins, nitric oxide, serotonin, and hormonal derangements, which may cause structural and functional changes in the splenoportal venous system [181],
4. The reduction in the size of an aneurysm is related to a decrease in splenic vein blood flow [176]. These observations suggest that the persistent stagnation of blood flow in the portal system may play a major role in the development of the SVA.

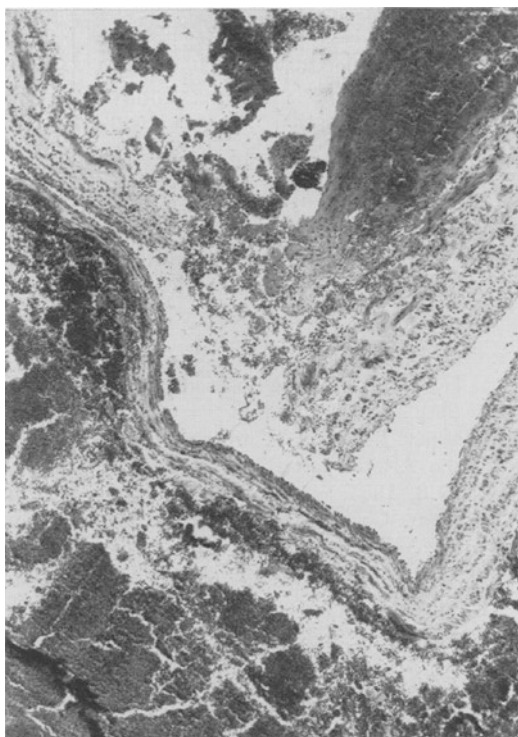
#### 24.4.4.2 Hemodynamic and Hormonal Changes in Pregnancy

An increase in cardiac output and blood volume, usually found in the later months of pregnancy, is an important factor in the precipitation of vascular accidents [92]. An increase in estrogen receptor expression in endothelial and vascular smooth muscle layers of arteries is associated with increased relaxation via endothelium-derived vasodilators and inhibition of  $\text{Ca}^{2+}$  entry into the vascular smooth muscle [182]. The increase in blood volume, hypertrophy, the dilation of the veins, and changes in venous pressure related to pregnancy seem to be involved in the pathogenetic mechanism [170]. Hemodynamic and hormonal changes may cause vascular alterations, which may weaken the vein wall (Fig. 24.24).

#### 24.4.4.3 Mechanical Factors

Lax perisplenic ligaments can lead to splenic torsion, resulting in splenic vein rupture (see Sect. 24.5).





**Fig. 24.24** Photomicrograph of a splenic vein showing an acute inflammatory reaction and fibrinoid alteration in the vein wall with perforation and surrounding bleeding. (Reproduced with permission from [133])

### 24.4.5 Clinical Presentation

Abdominal venous aneurysms, including SVA, are usually incidental findings. However, 75% of nonpregnant patients had clinical complaints: 50% had abdominal pain, and all had abdominal fullness and hepatic dysfunction. One patient presented in a state of shock with intra-abdominal bleeding. The similarity between spontaneous perforation of the splenic vein and SAA rupture is striking in many aspects: symptoms, signs, the lucid interval of amelioration of symptoms, occurrence in late pregnancy, and the therapeutic indications in both conditions [131, 133, 183–185].

Depending on the mechanism, extent, and location of the splenic vein rupture, the severity of the bleeding can be variable. If significantly severe, upper abdominal pain and nausea are followed by collapse. The patient recovers after several minutes, but the abdominal pain continues.



**Fig. 24.25** Hematoma and spontaneous rupture at the splenic vein 3 cm from the splenic hilum on autopsy in the fifth month of pregnancy. (Reproduced with permission from [169])

The pain can be present on the top of the left (*Kehr's sign*) or both shoulders [133]. With slower bleeding or early hospital referral, collapse from hemodynamic shock could be avoided.

### 24.4.6 Differential Diagnosis

See Sect. 24.3.6.

### 24.4.7 Diagnosis

In the general population, angiography is the imaging of choice for diagnosing a visceral aneurysm (rupture) if the patient is hemodynamically stable. In selected cases, it is also a treatment modality. Contrast-enhanced abdominal CT can reveal the diagnosis in a hemodynamically stable patient. Sometimes, the diagnosis is made intra-operatively or during autopsy (Fig. 24.25) [102, 169].

### 24.4.8 Treatment

#### 24.4.8.1 Surgical Treatment

The natural course of non-ruptured SVA is uncertain; therefore, when patients in the general population are asymptomatic, treatment is controversial. To avoid the risk of rupture, SVA of 1–2 cm should be followed up regularly with abdominal CT, abdominal MRI, or transabdomi-



nal color Doppler US. If inflammation is present from chronic pancreatitis, SVA should be treated surgically due to the increased risk of rupture [178]. However, the most secure recommendation is that in pregnancy, even the smallest SVA should be treated surgically [166].

Because of the already damaged vein wall, repair of the vein should be avoided. Control of bleeding, ligation of the vein, meticulous hemostasis, and splenectomy are the appropriate treatments. Splenectomy has long been advocated to correct the pancytopenias from the hypersplenism associated with portal hypertension in cirrhotic patients. However, even though this intervention may correct the hematological status, it rarely changes the course of the underlying disease. The standard management of SVA rupture remains emergent SVA resection, distal pancreatectomy, splenectomy, and splenorenal shunt [179].

## 24.4.9 Prognosis

### 24.4.9.1 Maternal Outcome

It is difficult to discuss the prognosis due to several patients with splenic vein rupture during pregnancy. Due to slower bleeding than from SAA rupture, the prognosis is better. Maternal mortality is almost nil, and all survived except mothers that died from preoperative exsanguination [133, 166, 167, 169, 170].

### 24.4.9.2 Fetal Outcome

Despite excellent maternal survival, fetal survival is poor. This is due to exsanguination, resulting in fetal distress and intrauterine fetal death. Only fetal survival recorded is in patients that presented postpartum [133, 166, 167, 169, 170].

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## 24.5 Splenic Torsion

### 24.5.1 Historical Perspective and Incidence

Splenic torsion is an exceedingly rare complication in pregnancy. Meek made the first case of successful splenectomy due to splenic torsion in

pregnancy in 1907 [186]. Only several cases are published during pregnancy and puerperium [186–189].

### 24.5.2 Etiopathogenesis

It is a complication of the wandering spleen, a rare condition characterized by increased splenic mobility due to the absence or laxity of its suspensory ligaments. When twisted on its pedicle, it may present as an acute abdomen [190]. It has also been reported with abdominal trauma, splenomegaly, nonspecific abdominal muscle laxity, and laxity resulting from the hormonal effects of pregnancy [191]. It has been suggested that the softening effect of pregnancy hormones on ligaments, the abdominal musculature, diminished peritoneal cavity volume as a result of the gravid uterus, and a maximal third-trimester increase in whole-blood volume might be the predisposing factors in pregnancy [187, 188]. A sudden decrease of the uterus after delivery or CS, especially of the enlarged spleen, can result in splenic torsion [187].

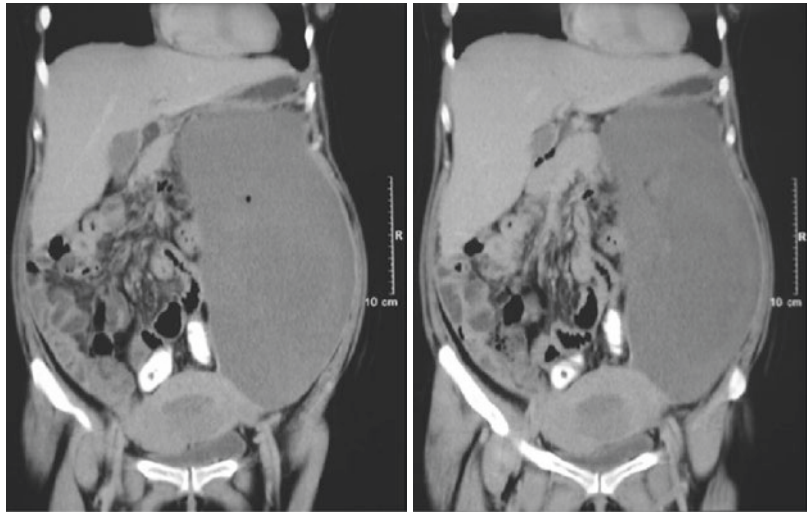
### 24.5.3 Clinical Presentation

Symptoms of splenic torsion vary depending on the degree of torsion. Mild torsion might manifest with chronic abdominal pain resulting from congestion; moderate torsion might manifest with severe intermittent abdominal pain related to intermittent rotation and derotation [25, 186, 187]. Severe and acute torsion presents symptoms and signs of acute abdomen [188, 191]. The palpable mass may be present. Primary diagnosis can be masked by presenting complications—hematemesis, acute pancreatitis, gastric volvulus, or pulmonary complications [187].

### 24.5.4 Differential Diagnosis

Intermittent moderate abdominal pain is sometimes attributed to other diseases [186], such as acute pancreatitis [192]. The most common preoperative differential diagnosis is splenic infarction, symptomatic/ruptures SAA, or SVA.

**Fig. 24.26** Post-cesarean section abdominal CT shows a huge loculated fluid collection, 10.5 × 18 × 25.5 cm, in the left anterolateral abdomen. Bilateral pleural effusion, rightward displacement of the bowel loops, and upward displacement of the spleen are also evident. (Reproduced with permission from [187])



### 24.5.5 Diagnosis

Preoperative diagnosis is difficult, and definitive diagnosis is commonly encountered during surgical exploration. Preoperative diagnosis can be suspected with the known splenic disease [187]. In such cases, thrombocytopenia and previous or new-onset anemia should raise suspicion [187].

Imaging methods can show splenic torsion or indirect signs of acute splenic disease, such as rupture with hemoperitoneum in the left upper quadrant or left hemiabdomen (Fig. 24.26).



**Fig. 24.27** A torted vascular pedicle of wandering spleen with infarcted, hypermobile spleen. (Reproduced with permission from [188] under the CC Attribution License)

### 24.5.6 Treatment

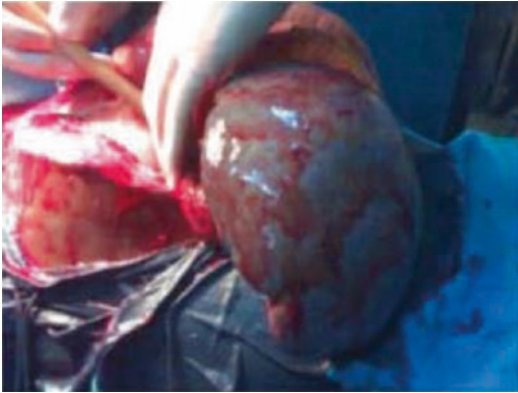
It is not clear whether splenectomy should be performed before pregnancy in cases of splenomegaly to prevent splenic torsion during pregnancy and postpartum [187].

#### 24.5.6.1 Surgical Treatment

Treatment is always surgical. Initial exploration is done by laparoscopy or laparotomy. The further procedure depends on the status of the spleen. If long-standing detorsion is present with infarction and gangrene of the spleen, splenectomy is indicated (Fig. 24.27). Detorsion with splenopexy is indicated with early exploration and vital spleen (Fig. 24.28).

#### 24.5.6.2 Prevention of Future Torsion

Intermittent torsion with underlying splenic pathology, such as autoimmune thrombocytopenic purpura, predisposes to further torsions. Therefore, splenectomy is indicated. Without underlying pathology, splenopexy can be done. The best timing is before pregnancy or symptomatic torsion during the second trimester. The second trimester carries the lowest risk of obstetric complications. With modern imaging techniques, the risk of future torsion (due to the enlarged or ectopic spleen) can be adequately estimated



**Fig. 24.28** Enlarged and vital spleen on its twisted pedicle at 28 weeks of pregnancy. (Reproduced with permission from [193])

before and during pregnancy. Another indication for splenectomy is external compression of the ureter (with or without hydronephrosis). MRI and MR angiography are sensitive and noninvasive techniques providing a stereoscopic evaluation of the hilar vessels of the spleen to make a safe prediction of the risk for torsion [194].

### 24.5.7 Prognosis

The prognosis depends on the severity and duration of splenic torsion. If operated on early, the prognosis is excellent. With maternal hemorrhagic shock, fetal mortality is likely [193].

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## Abstract

Trauma complicates 7% of pregnancies and is the leading nonobstetric cause of death among pregnant women. The most common traumatic injuries are motor vehicle crashes, assaults, falls, and domestic violence. Approximately 90% of traumatic injuries during pregnancy are classified as minor, yet 60–70% of fetal losses after trauma result from minor injuries. Penetrating trauma most commonly includes the growing uterus and the fetus, protecting maternal intra-abdominal organs. In such cases, especially stab wounds, the maternal outcome is excellent. In minor trauma, tocodynamometric monitoring of 4 h is recommended. It is extended to 24 h if indicated. Ultrasonography has low sensitivity but high specificity for placental abruption. The Kleihauer-Betke test should be performed after major trauma to determine the degree of fetomaternal hemorrhage, regardless of Rh status. A maternal left lateral tilt of 30° improves the effectiveness of cardiopulmonary resuscitation. Unique aspects of advanced cardiac life support include early intubation, removal of all uterine and fetal monitors, and perimortem cesarean delivery within 4–5 min from maternal death. Proper seat belt use reduces the risk of maternal and fetal injuries in motor vehicle crashes. The lap belt should be placed as low as possible under the

protuberant portion of the abdomen, and the shoulder belt should be positioned off to the side of the uterus, between the breasts, and over the midportion of the clavicle. All women of childbearing age should be routinely screened for intimate partner violence.

## 25.1 General Considerations

### 25.1.1 Incidence

Injuries resulting in an emergency department visit occur in 3–7% of pregnancies [1–4]. Most reports claim 0.3–0.4% of pregnant women require hospital admission because of trauma, some even 0.9% [1, 2, 4–7]. Significant variations exist even within the country. For example, in Burkina Faso: 0.02%, 0.3%, and 0.9% [7–9].

Blunt trauma is the most common type among pregnant women accounting for 69% of the total cases of traumas, whereas penetrating trauma accounts for only 1.5% [10]. In declining incidence, the cause of maternal trauma is motor vehicle accident (MVA), followed by falls, interpersonal violence, and burns [3, 4, 7, 10–16], although some claim the falls are the most common [17, 18]. In the USA, the annual crash rate for pregnant women is at least 13/1000 person-years compared to 26/1000 person-years among nonpregnant women [19]. Pregnant patients

**Table 25.1** Estimated incidence/prevalence of injury by type of trauma during pregnancy

| Mechanism of injury             | Estimated incidence/prevalence in pregnancy | Estimated incidence/prevalence outside of pregnancy |
|---------------------------------|---------------------------------------------|-----------------------------------------------------|
| Motor vehicle crashes           | 207/100,000 live births                     | 1104/100,000 women <sup>a</sup>                     |
| Falls and slips                 | 48.9/100,000 live births                    | 3029/100,000 women                                  |
| Burns                           | 0.17/100,000 person-years                   | 2.6/100,000 person-years                            |
| Accidental poisoning            | N/A                                         | N/A                                                 |
| Domestic violence               | 8307/100,000 live births                    | 5239/100,000 women <sup>a</sup>                     |
| Suicide <sup>b</sup>            | 2/100,000 live births                       | 8.8/100,000 population <sup>a</sup>                 |
| Homicide                        | 2.9/100,000 live births                     | 2.3/100,000 women                                   |
| Penetrating trauma <sup>c</sup> | 3.27/100,000 live births <sup>a</sup>       | 3.4/100,000 women <sup>a</sup>                      |
| Toxic exposure                  | 25.8/100,000 person-years                   | 115.3/100,000 person-years                          |

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The incidence of burns during pregnancy is limited to most severe cases admitted to burn units and referral centers. The rate of accidental poisoning during pregnancy is difficult to calculate. Domestic violence incidence includes all forms of partner violence: sexual, physical, and psychological. *N/A* not available

<sup>a</sup>Rates calculated using 2009 US data from Centers for Disease Control and Prevention

<sup>b</sup>Rates exclude attempted suicides. The *attempted* suicide rate during pregnancy is approximately 40/100,000 pregnancies and during the postpartum period is 43.9/100,000 live births

<sup>c</sup>Rates include only causes leading to fatality

represent 1.5–3.8% of all collision-related MVA [20, 21]. MVAs are responsible for about 50% of nonpenetrating abdominal wounds, often with severe trauma and often associated with other injuries [11, 15, 16]. Pregnant women involved in MVA are more likely to be in a motor vehicle than a bicyclist or pedestrian struck by a car than nonpregnant women [20]. Approximately 6–7% of all pregnant women experience physical trauma in the USA, accounting for 20% of maternal mortality [5, 15, 22–25]. Significant trauma occurs in 8% of pregnant women. Most trauma accidents (>50%) occur during the second and third trimesters [11, 17]. Table 25.1 shows the estimated incidence/prevalence of injury by type of trauma during pregnancy. Penetrating injuries constitute a greater proportion of injuries in inner-city centers [27, 28].

The pattern of severe injuries in pregnant women differs from that of nonpregnant trauma patients: injuries to the abdomen are more common than injuries to the head and chest [7].

## 25.1.2 Risk Factors

### 25.1.2.1 Maternal Risk Factors

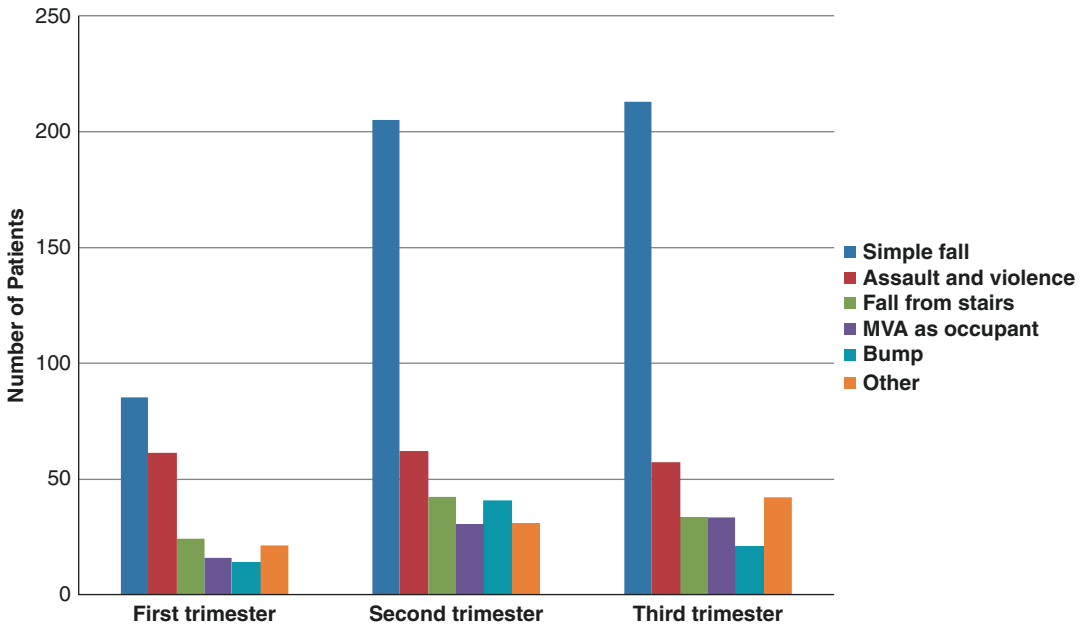
Major risk factors for maternal trauma include maternal and external risk factors [20, 21, 29–34] presented in Table 25.2.

**Table 25.2** Risk factors for maternal trauma during pregnancy

| Maternal factors                        | External factors                       |
|-----------------------------------------|----------------------------------------|
| Age <25 years                           | Low socioeconomic status               |
| African–American/Hispanic race          | Work outside the home                  |
| Illicit drugs/alcohol/smoking           | Medicaid insurance                     |
| Domestic violence                       | Traffic/transportation law/regulations |
| Noncompliance with proper seat belt use | The severity of a court sentence       |
| Epilepsy or other seizures              |                                        |
| Overweight and obesity                  |                                        |
| Birth rates                             |                                        |

Compared to nonpregnant trauma patients, pregnant women are younger and less severely injured [35]. Changed attitudes to pregnancy have resulted in women increasingly being involved in social, commercial, and professional activities virtually throughout their pregnancies, thus exposing themselves to a risk of accidental injury similar to that in the nonpregnant population. Pelvic ligamentous laxity and the protuberant abdomen of pregnancy contribute to gait instability, predisposing the pregnant woman to falls, especially with pregnancy progression. The prominent abdomen, especially toward the term, becomes vulnerable to any form of trauma. Therefore, even minor accidental injury is more





**Fig. 25.1** Distribution of maternal trauma by trimester in Turkey. The highest number of trauma cases were obtained during the second trimester. The falls are the most com-

mon etiology of blunt trauma. Simple fall was the most dominant in all trimesters. (Reproduced with permission from [36] under the CC Attribution License)

common during pregnancy than at any other time in adult life.

The impact of mind-altering substances is significant, with 19.6 and 12.9% of the USA pregnancy-related trauma associated with illicit drugs or alcohol, respectively [21]. Intoxicants are found in up to 45% of the pregnant population involved in MVAs [31]. Intoxicated patients have significantly lower seat belt use than sober patients (22% vs. 46%, respectively) [31].

Mothers who reported an injury during pregnancy were more likely to be aged <18 years vs. 18–29 years and less likely to be aged ≥30. They were more likely to use alcohol during pregnancy, smoke, have epilepsy, and be employed than mothers who did not report an injury [17]. The distribution by trimesters according to the intention and cause is presented in Fig. 25.1. However, knowledge of characteristics specifically associated with injury to pregnant women can help identify women who may be at higher risk for experiencing an injury during pregnancy and can potentially inform the development of prevention programs for women to reduce the

risk of injury during pregnancy. These characteristics have been associated with adverse pregnancy outcomes, such as alcohol with fetal alcohol syndrome, smoking with orofacial defects and preterm delivery, and obesity with neural tube defects and Cesarean section (CS). Therefore, efforts to modify these exposures may have multiple positive impacts. For example, preventing alcohol use during pregnancy could reduce the fetal risk from alcohol and maternal injuries, which can adversely affect pregnancy outcomes. It is recommended that pregnant women be screened for alcohol use at their first prenatal visit.

### 25.1.3 Maternal Changes Relevant to Trauma

#### 25.1.3.1 Maternal Anatomy and Physiology

Pregnancy should be considered in female trauma patients of reproductive age. Pregnancy causes anatomic and physiological changes involving

**Table 25.3** Physiological changes in pregnancy relevant to trauma

| System           | Changes                                                                        | Impact                                                     |
|------------------|--------------------------------------------------------------------------------|------------------------------------------------------------|
| Cardiovascular   | ↓ Peripheral vascular resistance                                               | Masking of initial signs of sepsis                         |
|                  | ↑ Heart rate                                                                   | Increased hypoperfusion                                    |
|                  | ↓ Arterial pressure                                                            |                                                            |
|                  | ↑ Cardiac output                                                               |                                                            |
| Blood            | ↑ Plasma volume                                                                | Greater reduction of oxygen supply to tissues              |
|                  | ↑ Red cell volume                                                              |                                                            |
|                  | Anemia                                                                         |                                                            |
| Respiratory      | ↑ Tidal volume                                                                 | Delayed physiological response to metabolic alkalosis      |
|                  | ↓ Residual volume                                                              | Impaired oxygenation                                       |
|                  | ↑ Minute ventilation by 30–40%                                                 |                                                            |
|                  | ↑ Respiratory center stimulation → ↑ respiratory rate                          |                                                            |
|                  | ↓ da PaCO <sub>2</sub>                                                         |                                                            |
| Renal            | Ureteropelvic dilation and ↓ ureteral pressure due to smooth muscle relaxation | Delayed identification of renal injury secondary to sepsis |
|                  | Flaccid bladder                                                                | Favorable to pyelonephritis                                |
|                  | ↑ Intravesical pressure due to the pregnant uterus weight                      |                                                            |
|                  | ↑ Vesicoureteral reflux                                                        |                                                            |
|                  | ↑ Renal plasma flow                                                            |                                                            |
|                  | ↑ Glomerular filtration rate                                                   |                                                            |
|                  | ↓ Urea and creatinine average values                                           |                                                            |
|                  | Asymptomatic bacteriuria                                                       |                                                            |
| Gastrointestinal | ↓ Muscle tone across the digestive tract                                       | ↑ Risk of bacterial translocation                          |
|                  | Delayed gastric emptying                                                       | ↑ Risk of aspiration pneumonia                             |
|                  | Diaphragm elevation by the pregnant womb                                       | ↑ Risk of cholestasis, hyperbilirubinemia, and jaundice    |
|                  | Changes in bile composition                                                    |                                                            |
|                  | ↑ Production of pro-inflammatory cytokines by Kupffer cells                    |                                                            |
|                  |                                                                                |                                                            |
| Coagulation      | ↑ Factors VII, VIII, IX, X, XII, Von Willebrand and fibrinogen                 | ↑ Risk of thrombotic events                                |
|                  | ↓ Protein S                                                                    | ↑ Risk of DIC                                              |
|                  | ↓ Fibrinolytic activity                                                        |                                                            |
| Genital          | ↓ Vaginal pH                                                                   | ↑ Risk of chorioamnionitis                                 |
|                  | ↑ Glycogen in vaginal epithelium                                               |                                                            |

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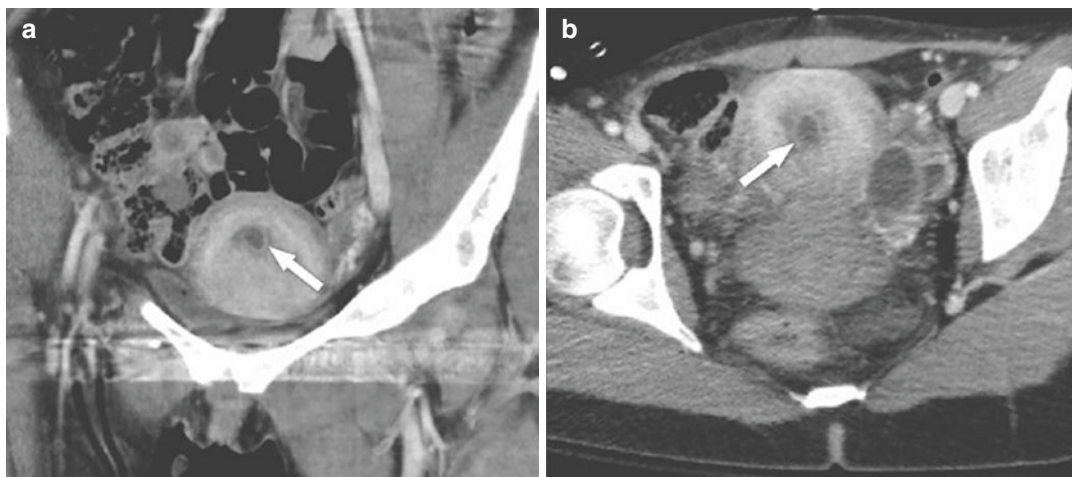
PaCO<sub>2</sub> arterial carbon dioxide partial pressure, DIC disseminated intravascular coagulation

nearly every organ system in the body, making the treatment of a pregnant trauma patient complex [37, 38]. Table 25.3 shows anatomic and physiological changes in pregnancy relevant to trauma.

These changes can alter the symptoms and signs of injury and may influence the interpretation of traumatized pregnant women's physical examination and laboratory results. It may affect the approach and the response to resuscitation

[37, 38, 40]. During the first trimester of pregnancy, the uterus is confined and protected by the bony pelvis (Fig. 25.2). It remains an intrapelvic organ until the 12th week of gestation when it rises and becomes an abdominal one.

In the first two trimesters, the uterus is additionally protected by the amniotic fluid, which acts as a hydraulic shock absorber, decreasing the force of the blow by transmitting it equally in all directions [42]. In the second trimester, the small



**Fig. 25.2** Uterus is protected by the bony pelvis and remains an intrapelvic organ until the 12th week of gestation. (a, b) CT images through the pelvis at 6 weeks and 4

days gestation show an early gestational sac within the endometrium (white arrows). (Reproduced with permission from [41])

fetus remains cushioned by a large amount of amniotic fluid. Later in pregnancy, the fetal head is fixed in the pelvis, and the buffering effect of the amniotic fluid decreases, making the head prone to injury. By the third trimester, the uterus is large and thin-walled [43]. The uterus and its contents have increased susceptibility to injury (penetration, rupture, placental abruption, and premature rupture of membranes). Some of the characteristics causing this increased susceptibility include the difference in elasticity between the uterus and placenta, which causes the uteroplacental interface to be subject to shear forces. It may lead to placental abruption [44]. Plasma volume increases throughout pregnancy, with a plateau at about 34 weeks. A lesser increase in red blood cells decreases hematocrit [37, 43]. The placental vasculature is maximally dilated and sensitive to catecholamine stimulation [37, 43, 44]. An acute decrease in the intravascular volume may result in a significant increase in uterine vascular resistance. This could cause a reduction in fetal oxygenation, even though the maternal vital signs can stay within a normal range [22, 37, 40, 44, 45].

Hemodynamic changes during pregnancy are relevant when dealing with injured pregnant patients. Increased cardiac output is noted after 10 weeks of gestation due to increased plasma

volume and decreased vascular resistance of the uterus and placenta. During the third trimester, the uterus and placenta receive 20% of cardiac output. A gradual increase in the cardiac rate, maximal in the third trimester, must be considered when evaluating the tachycardic response to hypovolemia. In the second trimester, there is a decrease in both systolic and diastolic blood pressure. The left lateral tilt may prevent hypotension [37, 43]. Increased progesterone levels in pregnancy increase tidal volume and minute ventilation.

Hypocapnia is common in late pregnancy. The diaphragm elevates, causing decreased residual volume. Maintaining adequate arterial oxygenation is essential in the resuscitation of injured pregnant patients because of increased oxygen consumption during pregnancy [37]. The cardiovascular changes during pregnancy complicate the evaluation of intravascular volume, blood loss assessment, and hypovolemic shock diagnosis [46]. Maternal hemodynamic measurements may not accurately reflect the status of the uteroplacental circulation. Animal studies have demonstrated that maternal heart rate and blood pressure may remain within normal ranges during a 20% acute blood loss or a gradual loss of 30–35% of estimated total blood volume [47]. Also, the unreliability of maternal blood pres-

sure and pulse rate in predicting fetal loss is documented [48]. Uterine vasculature is maximally dilated during pregnancy minimizing autoregulation. Therefore, uterine blood flow depends entirely on maternal mean arterial blood pressure (MAP). Pregnancy represents a state of accelerated but compensated intravascular coagulation, which has both advantages and disadvantages for the pregnant trauma victim [46]. Increased levels of coagulation factors may improve hemostasis following trauma. At the same time, parturients remain at increased risk for thromboembolic complications during immobilization. Because buffering capacity diminishes during pregnancy, pregnant trauma victims rapidly develop metabolic acidosis during hypoperfusion and hypoxia.

Gastric emptying is prolonged in pregnancy. Therefore, in the emergency setting, early gastric tube decompression prevents aspiration. In the third trimester, as the uterus enlarges, the bowel is pushed upward, mainly in the upper abdomen [43]. Therefore, in blunt trauma, the bowel is relatively protected while the uterus and its contents (fetus, placenta) are more exposed. However, penetrating trauma to the upper abdomen can cause complex intestinal injury [37].

Physiological dilatation of the renal calyces, pelvis, and ureters is noted and should be considered when dealing with pelvic and abdominal trauma cases. During pregnancy, the pituitary gland increases in size. Shock can cause necrosis of the anterior pituitary gland, resulting in pituitary insufficiency. The symphysis pubis and the sacroiliac joints widen and should be considered when interpreting pelvic X-rays. In the vertex presentation, the fetal head is usually located in the pelvis, while the rest of the body is above the pelvic brim. Pelvic fractures in late gestation may result in fetal head injury (see Chap. 5) [43]. Differentiating between head trauma with convulsions and eclampsia (hypertension, proteinuria, and peripheral edema) as a cause of seizures is crucial [43].

There is an increase in the level of maternal plasma fibrinogen, factors II, VII, VIII, IX, and X, and a decrease in plasminogen activator lev-

els. This is important in trauma where hypercoagulability and the risk of deep venous thrombosis are already increased.

The clinician should know “normal” laboratory values during pregnancy (Table 25.4). The findings of normal nonpregnant values of  $p\text{CO}_2$  or fibrinogen in the pregnant patient are concerning.

### 25.1.3.2 The Impact of Pregnancy on Trauma Mortality

The tenth revision of the International Classification of Diseases (ICD-10) defines maternal death as “the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to, or aggravated by, the pregnancy or its management but not from accidental or incidental causes” [50].

Hormonal influences on outcomes after trauma have contradictory results. In experimental models, relatively high estrogen (and progesterone) levels have beneficial immunomodulatory, vasodilatory, and survival effects after trauma [51, 52]. If a hormone-dependent survival benefit exists, pregnant women with higher estrogen and progesterone levels might exhibit lower mortality than similarly injured nonpregnant women. Pregnant trauma patients are approximately 40% less likely to die than their nonpregnant counterparts [53]. This survival benefit was evident in younger women, suggesting a possible additive beneficial effect of youth and pregnancy. There was no survival benefit in pregnant women when severely injured patient subgroups were compared (ISS >15, severe head injury, severe abdominal injury, or patients in hypotensive shock). This suggests that whatever advantage pregnancy may confer may be limited. Also, mortality is increased in pregnant patients with severe abdominal injuries. This may partly be related to placental abruption contributing to internal bleeding [53].

Analysis of data from the *National Trauma Data Bank* (1994–2001) of 1195 pregnant trauma patients showed a crude mortality rate of 1.4% compared to 3.8% for nonpregnant patients

**Table 25.4** Normal laboratory values during pregnancy

| Test | Unit                | Normal value           | 13–20 weeks  | 21–28 weeks  | 29–34 weeks | 35–42 weeks  | Partus       | Partus + 1   | Partus + 2  |
|------|---------------------|------------------------|--------------|--------------|-------------|--------------|--------------|--------------|-------------|
| ALT  | μkat/L              | 0.17–0.75 <sup>a</sup> | ←            | 0.14–0.60    | ←           | ←            | 0.08–0.70    | ←            | 0.13–0.97   |
| ALB  | g/L                 | 36–48 <sup>a</sup>     | ← 32–43      | ←            | 30–40       | ←            | ←            | ← 25–38      | ←           |
| ALP  | μkat/L              | 0.58–1.75 <sup>a</sup> | ← 0.66–1.53  | ← 0.73–1.91  | ← 0.94–2.66 | ← 1.47–4.49  | ← 1.82–6.15  | ← 1.60–4.50  | ←           |
| AST  | μkat/L              | 0.25–0.58 <sup>a</sup> | ←            | 0.27–0.67    | ←           | ←            | ← 0.30–1.87  | ← 0.37–1.29  | ←           |
| BIL  | μmol/L              | 5–25 <sup>a</sup>      | ←            | ←            | ←           | 2–13         | ←            | ←            | ←           |
| CHOL | mmol/L              | 2.9–6.1 <sup>a</sup>   | ←            | ←            | ←           | 3.7–9.5      | ←            | ←            | ←           |
| HDL  | mmol/L              | 1.0–2.7 <sup>a</sup>   | ←            | ←            | ←           | 1.0–3.0      | ←            | ←            | ←           |
| LDL  | mmol/L              | 1.2–4.3 <sup>a</sup>   | ←            | ←            | ←           | 1.2–6.0      | ←            | ←            | ←           |
| VLDL | mmol/L              | <0.5 <sup>b</sup>      | ←            | ←            | ←           | 0.3–2.0      | ←            | ←            | ←           |
| CRP  | mmol/L              | <10 <sup>b</sup>       | ←            | 10–300       | ←           | ←            | ← 10–424     | ← 40–900     | ←           |
| CREA | mmol/L              | 50–90 <sup>a</sup>     | ←            | 43–74        | ←           | ←            | 44–87        | ←            | ←           |
| HCT  | l                   | 0.35–0.46 <sup>a</sup> | ←            | ←            | 0.31–0.42   | ←            | ←            | ←            | ←           |
| HGB  | g/L                 | 117–153 <sup>a</sup>   | ←            | 112–146      | ←           | ←            | ← 108–156    | ← 95–148     | ←           |
| IRON | μmol/L              | 10–50 <sup>a</sup>     | ←            | 7–35         | ←           | ←            | ← 4–28       | ←            | ← 4–21      |
| TIBC | %                   | 10–50 <sup>a</sup>     | ← 7–47       | ←            | 5–41        | ←            | ← 5–32       | ←            | ← 5–23      |
| LDH  | μkat/L              | 1.8–3.4 <sup>a</sup>   | ←            | 1.9–3.1      | ←           | ←            | ←            | 2.1–5.1      | ←           |
| WBC  | 10 <sup>9</sup> /L  | 3.5–8.8 <sup>a</sup>   | ←            | 6.1–14.1     | ←           | ←            | ← 8.2–25.8   | ← 7.2–21.4   | ←           |
| BAS  | 10 <sup>9</sup> /L  | 0.00–0.20 <sup>b</sup> | ←            | 0.01–0.07    | ←           | ←            | ←            | 0.01–0.15    | ←           |
| EOS  | 10 <sup>9</sup> /L  | 0.00–0.50 <sup>b</sup> | ←            | ←            | 0.02–0.41   | ←            | ←            | ←            | ←           |
| LYMP | 10 <sup>9</sup> /L  | 0.70–4.80 <sup>b</sup> | ←            | 1.08–3.06    | ←           | ←            | ←            | 1.00–4.04    | ←           |
| MONO | 10 <sup>9</sup> /L  | 0.00–1.10 <sup>b</sup> | ← 0.26–0.72  | ← 0.27–0.77  | ← 0.26–0.94 | ← 0.30–0.99  | ← 0.29–1.17  | ← 0.30–1.25  | ← 0.30–0.97 |
| NEUT | 10 <sup>9</sup> /L  | 1.80–7.40 <sup>b</sup> | ← 3.95–11.60 | ← 4.82–23.42 | ← 0.30–0.97 | ← 5.39–14.73 | ← 3.95–11.60 | ← 4.82–23.42 | ← 0.30–0.97 |
| MCH  | pg/cell             | 27–33 <sup>a</sup>     | ←            | ←            | ←           | 27.4–34.6    | ←            | ←            | ←           |
| MCHC | g/L                 | 317–357 <sup>a</sup>   | ←            | ←            | ←           | 334–37.4     | ←            | ←            | ←           |
| MCV  | fL                  | 82–98 <sup>a</sup>     | ←            | ←            | ←           | 78–96        | ←            | ←            | ←           |
| PLT  | 10 <sup>9</sup> /L  | 145–390 <sup>a</sup>   | ←            | 167–406      | ←           | ←            | 150–390      | ←            | ←           |
| K    | mmol/L              | 3.5–4.4 <sup>a</sup>   | ←            | ←            | 3.1–4.2     | ←            | ←            | ←            | ←           |
| RBC  | 10 <sup>12</sup> /L | 3.90–5.20 <sup>a</sup> | ←            | 3.45–4.70    | ←           | 3.56–4.88    | ←            | 3.13–4.80    | ←           |
| Na   | mmol/L              | 137–144 <sup>a</sup>   | ←            | ←            | 135–142     | ←            | ←            | ←            | ←           |
| TSH  | mIU/L               | 0.4–4.0 <sup>b</sup>   | ←            | 0.3–4.0      | ←           | ←            | ←            | 0.8–6.2      | ←           |
| FT4  | pmol/L              | 10.3–23.2 <sup>b</sup> | ←            | ←            | 10.0–16.3   | ←            | ←            | ←            | ←           |
| TRAN | μmol/L              | 24–48 <sup>b</sup>     | ← 27–52      | ← 31–58      | ← 36–61     | ← 38–68      | ← 38–70      | ← 33–64      | ← 34–61     |
| TRIG | mmol/L              | 0.45–2.60 <sup>a</sup> | ← 0.76–2.49  | ← 0.87–3.15  | ← 0.98–3.59 | ← 1.33–4.72  | ← 1.25–4.94  | ← 1.22–4.06  | ← 1.19–4.57 |
| T3   | nmol/L              | 1.0–2.6 <sup>b</sup>   | ←            | ←            | 1.5–3.5     | ←            | ←            | ←            | ←           |
| BUN  | mmol/L              | 3.2–8.1 <sup>a</sup>   | ←            | ←            | 1.7–4.9     | ←            | ←            | ←            | ←           |
| URIC | μmol/L              | 155–350 <sup>a</sup>   | ← 110–267    | ← 120–296    | ← 124–330   | ← 150–390    | ← 170–437    | ← 185–450    | ← 190–459   |

\*Normal non-pregnant values are listed according to <sup>a</sup>(23, 24) or <sup>b</sup>local recommendation. The test abbreviation is listed in Table 25.1.

Reproduced with permission from [49]

( $p < 0.001$ ) [21]. Another smaller study found that “pregnancy does not increase maternal mortality from trauma” and that the most frequent cause of death in injured pregnant patients was head injury [54]. However, there is no proof that estrogen and progesterone are responsible for the survival advantage of pregnant patients. Probably hemodynamic changes are responsible and closer observation of pregnant than nonpregnant patients.

### 25.1.4 Prehospital Management

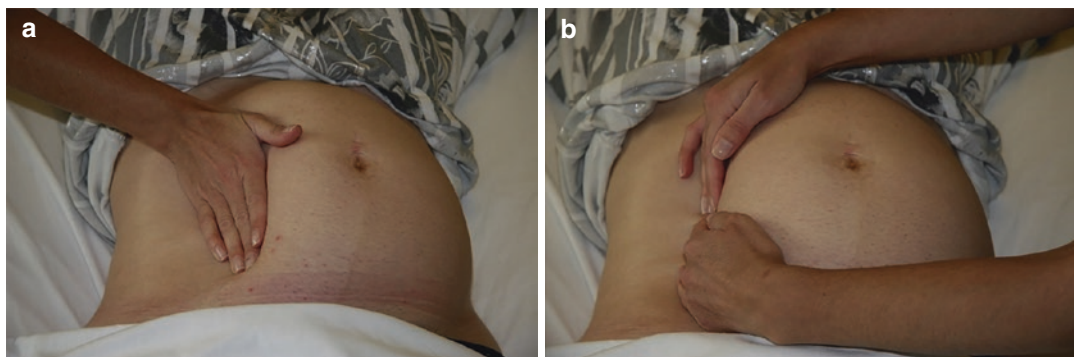
Prehospital management is the initial key to the survival of both the mother and fetus. Pregnancy is considered a triage criterion for transport to a trauma center by the *American College of Surgeons Committee on Trauma*. Whenever possible, transportation should be to a center that can provide obstetrical care, as long-term monitoring is usually required. Goodwin and Breen [55] proved in a landmark contribution in 1990 that in addition to the accepted *Advanced Trauma Life Support* (ATLS) guidelines (first five on the list)

for the *transfer of patients to level I trauma centers*, there are four additional:

- Glasgow Coma Score <14,
- Respiratory rate <10/min or >29/min,
- Systolic blood pressure <90 mmHg,
- Revised Trauma Score <11,
- Anatomy or mechanism of injury,
- Pulse >110 bpm,
- Chest pain,
- Loss of consciousness,
- Third trimester.

These criteria are particularly useful in mass casualty triage of patients in adjunction to pre-hospital trauma scoring systems. Upon initial assessment, *Emergency Medical Services* (EMS) should follow standard protocols like extrication with spinal immobilization and resuscitation as outlined in the ATLS guidelines. The decision to intubate the patient in the field is mainly unaffected by pregnancy (see Chap. 2).





**Fig. 25.3** Left lateral uterine displacement using (a) one-handed technique and (b) two-handed technique. (Reproduced with permission from [57])

After delivery, the neonatologist might find a flaccid, apneic infant. Hence, it is pertinent to relate any prehospital medication use by EMS to the receiving institution and trauma team. The potentially catastrophic consequences of the patient losing her airway in the field or during transport usually justify minor risks associated with paralytic and induction agents. An early and definite airway is the safest option.

Avoiding supine hypotension syndrome (uterocaval compression) should be a crucial part of initial resuscitative measures in pregnant trauma patients. Placing the patient on a backboard with a 15° angle to the left should be employed beyond 20 weeks of gestation. Significantly decreased cardiac output of up to 60% due to uterocaval compression leads to prolonged resuscitation with increased acidosis and vasopressor requirements [56]. Below 24 weeks, *manual left lateral displacement* might be sufficient. There is one-handed (Fig. 25.3) and two-handed (Fig. 25.3) technique according to the *American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care* from 2010 [58].

In gestations of >24 weeks, a 30° lateral tilt is recommended (Fig. 25.4). Although this reduces the efficacy of CPR compared to the supine position, in the pregnant patient, the slightly reduced effectiveness of chest compressions is outweighed by improved cardiac preload and overall cardiac output [56]. Therefore, the *Eastern*



**Fig. 25.4** Patient in a 30° left lateral tilt using a firm wedge to support the pelvis and thorax in gestations of >24 weeks. (Reproduced with permission from [57])

*Association for Surgery and Trauma* (EAST) guidelines recommend a left lateral tilt of at least 15° during the initial phase of resuscitation. The left lateral tilt, achieved by placing a wedge under the right flank and hip, displaces the uterus to the left side.

Placement of a rigid backboard in the supine position might not be tolerable for third-trimester gravida. The increased work of breathing due to increased diaphragmatic splinting might lead to respiratory failure. In this circumstance, transport in a 30° reversed Trendelenburg position seems acceptable [16]. For IV access routes in pregnant trauma patients, femoral access should be avoided. Because of the risk of uterocaval compression, the distribution of medications or fluids

might be significantly altered when using the femoral route in pregnant patients.

Pregnant females should be transported rapidly to a designated trauma center with facilities for managing the mother and fetus. The transfer should occur rapidly, even in minor trauma, because of the high rate of fetal demise. Paramedics should seek information regarding pregnancy from female patients of childbearing age. A distended abdomen may be due to a gravid uterus or intra-abdominal bleeding.

*For pregnant women in cardiac arrest, high-quality CPR with manual uterine displacement, early ALS, and delivery of the fetus, if an early return of spontaneous circulation is not achieved, remain key interventions. (European Resuscitation Council Guidelines [59])*

A left lateral tilt position can be utilized even with a suspected spinal fracture. Oxygen supplementation by nasal cannula or face mask should be routine. If prehospital transfusion is required, O-negative blood should be used whenever possible.

With military antishock trousers used, it is contraindicated to inflate the abdominal portion of this device for pregnant women. This maneuver reduces uterine perfusion and can increase the cardiac workload.

Appropriate personnel must be present or readily available in the emergency room when the emergency vehicle arrives. A team should include a neonatologist, anesthesiologist, trauma surgeon, sonographer, and staff radiologist. If a pelvic fracture or bleeding is suspected, a senior interventional angiographer should be on standby.

## 25.2 Anesthetic Management

See Chap. 2.

## 25.3 Blunt Trauma

*If a man strikes a man's daughter and brings about a miscarriage, he shall pay ten shekels of silver for her miscarriage. And if that woman dies, they shall put his daughter to death.*

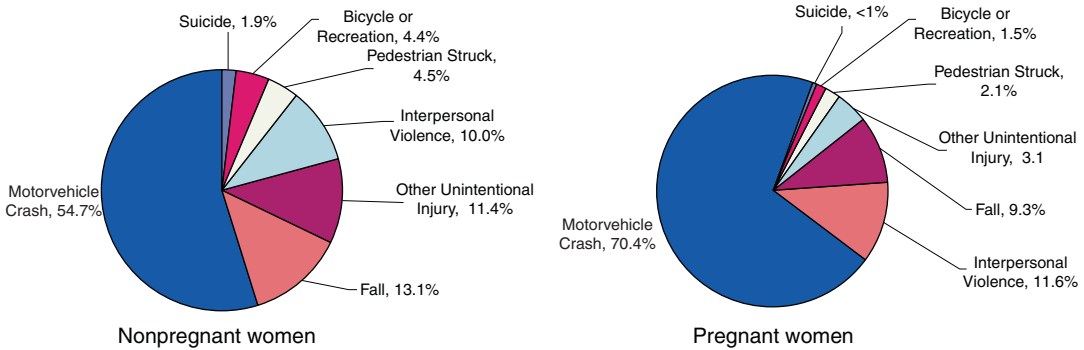
(The Code of Hammurabi, 2250 BC)

### 25.3.1 Historical Perspective

The assumption that a causal relation exists between external trauma and interruption of pregnancy is proposed by Assyrians (The Code of Hammurabi) in about 2250 BC [60]. As MVA is less than 150 years old, only falls and domestic violence could be the cause thousands of years ago. One of the first descriptions, not completely confirmed, is the domestic violence of the emperor Nero or Nero Claudius Caesar Augustus Germanicus (15 December 37–9 June 68 AD) to his second wife Poppaea Sabina (AD 30–AD 65). According to Suetonius, while awaiting the birth of her second child, she quarreled fiercely with Nero over his spending too much time at the races. In a sudden burst of rage, Nero kicked her in the abdomen, causing her death [61]. Other historians propose that Poppaea may have died due to the complications of miscarriage or childbirth [62]. It was known that abdominal trauma causes a miscarriage that even Avicenna (III, XXI, 212) and Rhases (Contin. VII, 2) recommended leaping from a height to produce abortion [63]. John Hill Brinton published the earliest scientific paper with cases of falls, blows, and assaults in 1884 [64].

### 25.3.2 Incidence

MVAs, domestic violence, and falls are the most common causes of blunt trauma in pregnancy [5, 15, 25, 30, 40, 45, 54, 65–67]. In Australia, blunt trauma accounts for nearly all trauma during pregnancy (MVA, injuries to occupants 65–75%; falls 10–20%; motor vehicle collision, injuries to pedestrians 5–15%; assault 1–10%) [68, 69], whereas in the USA, penetrating injuries account



**Fig. 25.5** Distribution of all-cause blunt trauma in nonpregnant and pregnant patients. (Reproduced with permission from [21])

for up to 10% [5]. Different mechanisms of maternal injury occur in pregnant women with blunt abdominal trauma compared with their nonpregnant counterparts. Because the gravid uterus changes the relative location of abdominal contents, force transmission may be altered in the pregnant abdomen [22, 44, 70]. The bony pelvis protects the uterus until 13 weeks of gestation. Fetal loss in the first trimester is not secondary to any direct uterine trauma but is usually due to maternal hypotension, hypoperfusion of the uterus, or the mother's death. Direct fetal injury is rare following blunt trauma, complicating <1% of all significant maternal trauma. The distribution of blunt trauma causes in nonpregnant and pregnant patients is compared in Fig. 25.5. MVAs were most common in both groups. Pelvic fractures in pregnancy represent 0.17–1.1% of all fractures [71, 72].

### 25.3.3 Motor Vehicle Accidents

#### 25.3.3.1 Introduction

Automobile crashes are the largest single cause of death for pregnant females and the leading cause of traumatic fetal injury mortality in the USA [19, 73]. Each year, 160 pregnant women die in MVAs, and an additional 800–3200 fetuses die when the mother survives in the USA [74, 75]. Among rear seat occupants, seat belt use can reduce the risk of death by at least 60% [76, 77]. One of the reasons for the mortality of rear seat passengers is the inappropriate handling of the safety belt.

#### 25.3.3.2 Incidence

From the 2000s, up to 3% of live births are linked to MVAs during pregnancy [19, 78–81], three times increase compared to 1955–1999 and two times higher than nonpregnant women [19]. In the USA (1975–1990), primarily because women drive more miles, the number of fatal crashes involving female drivers have increased by 62% [82]. Identifying pregnancy status from crash and medical records is not always easy for crash investigators because early pregnancy cases may not be known or reported. Further, many women are not interviewed directly, relying on written records that may or may not exist, especially for events that often do not result in hospital visits. Also, the methods for determining pregnancy and the completeness and accuracy of pregnancy status in the National Automotive Sampling System/Crashworthiness Data System (NASS/CDS) have not been externally validated. Furthermore, NASS/CDS coding rules state that when pregnancy status is unknown, cases are to be assigned to the “female not reported pregnant” category [83]. There is evidence from a statewide injury inpatient study that the hospitalized crash injury rate of pregnancy-associated cases is not lower compared to that of all women of reproductive age (even after a length of stay adjustment) [35].

#### 25.3.3.3 Mechanisms of Uterine and Fetal Trauma

The experimental research on the Savannah Baboon (*Papio cynocephalus*) was chosen because the uterine and placental anatomy are similar to humans [84]. The injuries observed are

similar to those reported in MVAs involving pregnant women [85, 86]. The fetal death rate of 8.3% among maternal animals impacted with three-point restraint was significantly lower than the 50% fetal death rate with lap belt restraint alone [87]. There is a remarkable increase in uterine pressure during impact. The maximum pressure was approximately ten times higher than during labor [88]. Simultaneous recordings of abdominal pressure during impact show that the uterus was not protected from rupture by an equal but opposing pressure within the surrounding abdominal cavity [89]. Nor was there a decrease in uterine pressure during impact when forward flexion was prevented by shoulder restraint or rearward-facing impact. The findings also indicate that the gravid uterus can withstand extraordinary pressures of short duration and that such pressures are produced by deceleration with or without body flexion. Maternal response to impact consisted of transient depression and bradycardia. The former resembled a mild cerebral concussion. Postimpact bradycardia occurs only with violent motion/deceleration of the body. This phenomenon is attributed to increased vagal tone secondary to acute hypertension in the carotid sinus. This effect can be abolished by atropine and occurs only when there is a rapid forward motion of the head and neck [90].

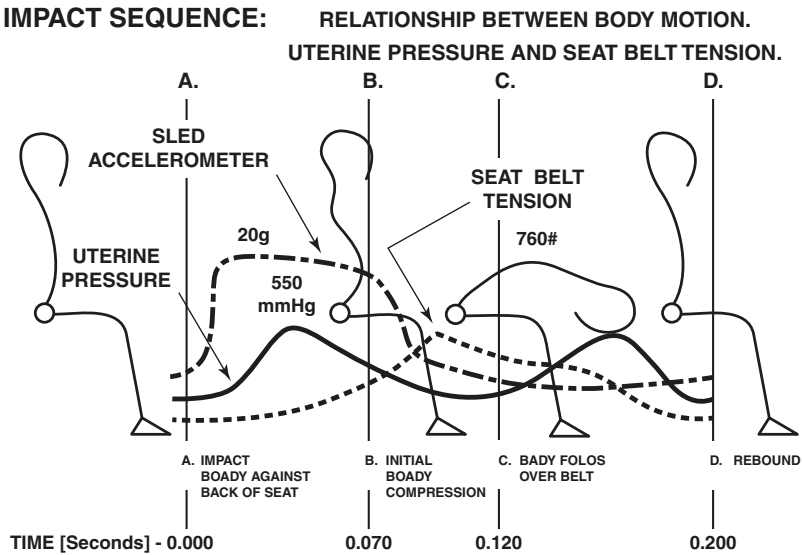
In experimental crashes, pregnant baboons were placed in two-point restraint in a Hyge sled

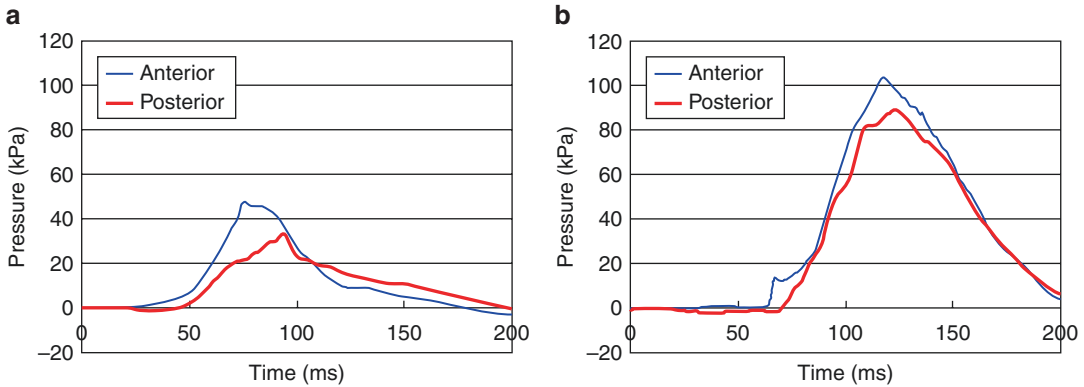
accelerometer, simulating an automobile crash under conditions of rapid deceleration (Figs. 25.6 and 25.7). A biphasic increase in intrauterine pressure is present. The first increase results from the sudden deceleration of the pelvis stopped by



**Fig. 25.6** The experimental research on the Savannah Baboon delivered the first knowledge of maternal and fetal physiology during and after motor vehicle accidents with belt restraints. (Reproduced with permission from [84])

**Fig. 25.7** Impact sequence (see text for details). (Reproduced with permission from [84])





**Fig. 25.8** Abdominal pressure in pregnant dummy during a frontal impact. (a) Anterior abdominal pressure in belted dummy peaked at about 60–70 ms from the start of impact and reached 1.4-fold the posterior pressure. (b)

Peak values of anterior and posterior abdominal pressure in an unbelted dummy were similar at about 120–130 ms when the forward excursion of the dummy was maximal. (Reproduced with permission from [95])

the lap belt. At the same time, the uterus continues to move forward, striking the anterior abdominal wall. This increases intrauterine pressure to 500 mmHg. Later during this crash sequence, the upper torso of the animal is thrown forward, essentially collapsing around the pregnant uterus, creating the second increase in intrauterine pressure, approaching 550 mmHg. In experiments with animals held by three-point restraints (*lap belt* and *shoulder belt*), the second increase in intrauterine pressure can be eliminated by preventing the torso from collapsing around the pregnant uterus. This decreases fetal mortality from 100% to 40% [91].

In 1996, the first pregnant crash dummy was developed as a feasibility project [92], and a computational model of the pregnant occupant [93] had numerous limitations. This computer model has been used to evaluate frontal crashes and has shown that local uterine compression is a critical factor in predicting placental abruption [94]. The anterior abdominal pressure peaks at 60–70 ms in a frontal impact of a belted dummy. At this point, the anterior abdominal pressure reaches 1.4-fold the posterior pressure (Fig. 25.8). Contact with the steering wheel is slight. The response is similar during the initial phase (i.e., backward excursion before a rebound) in the rear impact tests (Fig. 25.9). The inertial loading is the dominant contributor to the pressure applied to the uterus. The maximal pressure generated because of inertial loading is

below 20 kPa. In an unbelted frontal impact (Fig. 25.8), the anterior and posterior abdominal pressure indicated similar peak values at the maximal forward excursion of the dummy. However, the maximal values of the pressure due to compression are higher (60–70 kPa) than those of inertial loading.

The direct compression of the abdomen caused by the steering wheel's rim is the major contributor to maximal abdominal pressure.

The distribution of impact direction according to the sitting position in crashes involving pregnant patients is presented (Fig. 25.10).

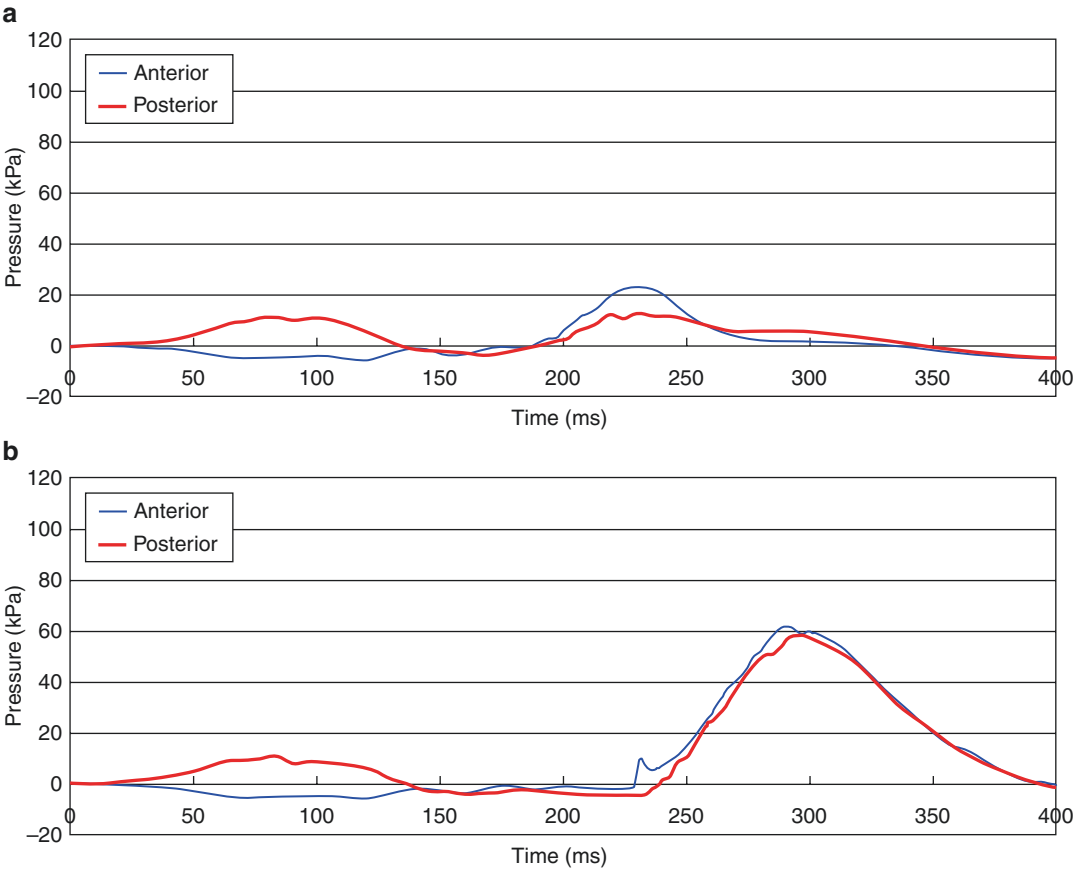
#### 25.3.3.4 The Seat Belt Use

*The primary way to protect the fetus is to protect the driver.*

(Lotta Jakobsson)

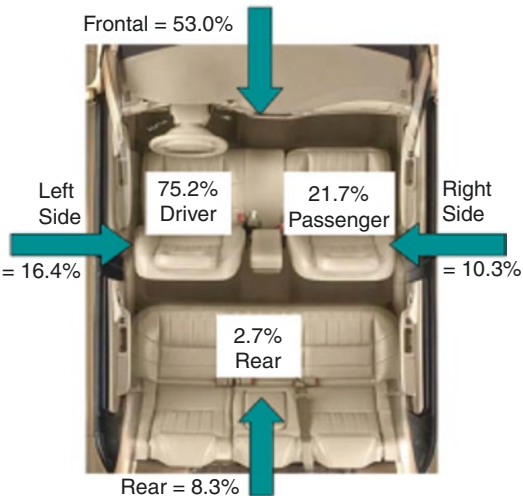
The first patented “safety” belt, designed to allow free movement and personal protection “for tourists,” was granted to Edward J. Claghorn in 1885. It consisted of an inner and an outer belt. Although no use of this belt has been reported, some of the first gasoline-engine vehicles have been equipped with restraining belts to keep passengers in their seats when traveling over the rough and rutted roads.





**Fig. 25.9** Abdominal pressure in pregnant dummy during a rear impact. (a) In belted dummy, anterior abdominal pressure was negative, whereas posterior pressure was positive during the initial phase (backward excursion before a rebound). (b) In the unbelted dummy, the

response during the second phase was similar to that of the unbelted frontal impact (Fig. 25.8) when the abdomen contacted the steering wheel. (Reproduced with permission from [95])



**Fig. 25.10** Occupant seating position and impact direction distributions for pregnant occupants. (Reproduced with permission from [96])

The seat belt is a safety harness designed to secure the occupant of a vehicle against harmful movement that may result from a collision or a sudden stop. As part of an overall occupant restraint system, seat belts are intended to reduce injuries by stopping the wearer from hitting hard interior elements of the vehicle or other passengers (the so-called second impact) and preventing the passenger from being thrown from the vehicle. Studies of MVA from the 1960s have shown that the single major cause of fatal injury was ejection from the vehicle [97]. The injury occurs with body ejection as it strikes the ground or is crushed by the vehicle. It was estimated that 80% of fatally injured MVA victims would have survived with the lap belts used [97]. As a result, lap-type seat belts become standard car equipment in the 1970s [85].

Seat belts could reduce injuries by 51% [98], lap belts by 35%, and diagonal belts by 60–80% [99]. Older studies claim a decrease in fatal MVA injuries from 35 to 80% [97, 100].

*Pregnant women should be encouraged to wear properly positioned safety restraints throughout while riding in automobiles. (American Medical Association Committee on Medical Aspects of Automotive Safety, 1972 [101])*

*The three-point restraint system (that places the lap belt under the abdomen and across the upper thighs and the shoulder belt between the breasts) should be used by pregnant occupants. (American College of Obstetricians and Gynecologists, 1983 [102])*

Safety belts are most effective in frontal collisions or when a vehicle attacks the barrier. Under the crash speed of about 50 km/h, the front is shortened by 50 cm, and seat belts take a significant part of the load. In sidelong collisions, the safety belts are much less efficient, and such collision leads to injuries to the head while hitting the side glass.

There currently are four principal configurations of seat belts in automotive use: the lap belt, the single diagonal belt, the three-point (the combination of lap and diagonal), and the double parallel combination of lap and double shoulder harnesses (Fig. 25.11).

A *lap belt* refers to a single belt across the anterior aspect of the pelvic structure; a *seat belt* refers to any combination of lap and torso restraint. Numerous variations exist, such as five-point, double vertical belts without lap belts and shoulder belts with inertia reels. Diagonal seat belts that run over the shoulder cause injuries primarily confined to the upper part of the trunk, such as a bruised chest, fractured ribs or sternum, and a lacerated liver. There are fewer head and

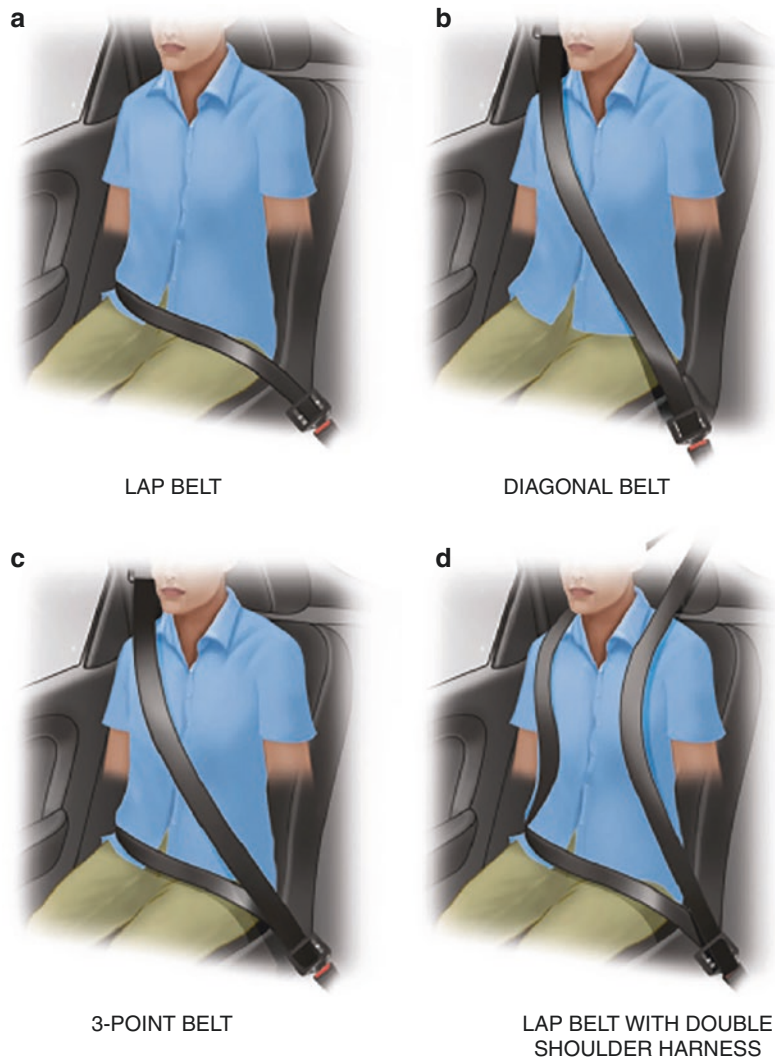
neck injuries with this belt type than with the lap type. The lap belt has an increased rate of injuries to the pelvis, lumbar spine, and abdomen. Bone injuries include a fracture of the pubis, separation of joints, and compression fracture of the lumbar spine, the so-called *fulcrum fracture* [103].

Using a lap belt alone may allow enough forward flexion and subsequent uterine compression to rupture the uterus. Placental abruption occurs when the strain in the uterine wall exceeds 60%. The risk of placental abruption is most prominent for high strains near the placenta, dramatically influenced by the lap belt position. Simulations have demonstrated that the vertical position of the lap belt increases fetal risk by 3× (Fig. 25.12).

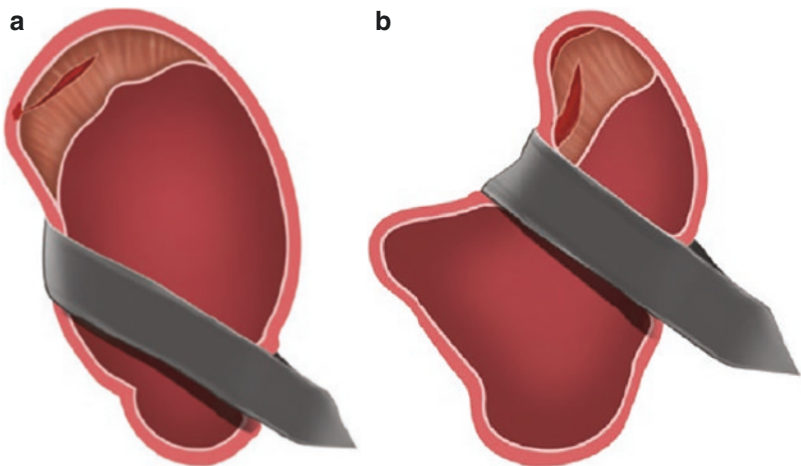
As the lap belt approaches the height of the placenta, which is located at the top of the uterus, the observed strain increases for a given crash pulse. Simulations with the lap belt directly loading the uterus at the placental location produced the highest recorded strain and may cause rupture [105]. Once the lap belt height is above the placenta, the strain decreases with the strain for the top belt position matching the recommended belt location. However, there is an increased risk to the mother with incorrect lap belt placement, including an increased head and chest injury rate. One of the first cases of placental abruption with a lap belt was in 1970 [106].

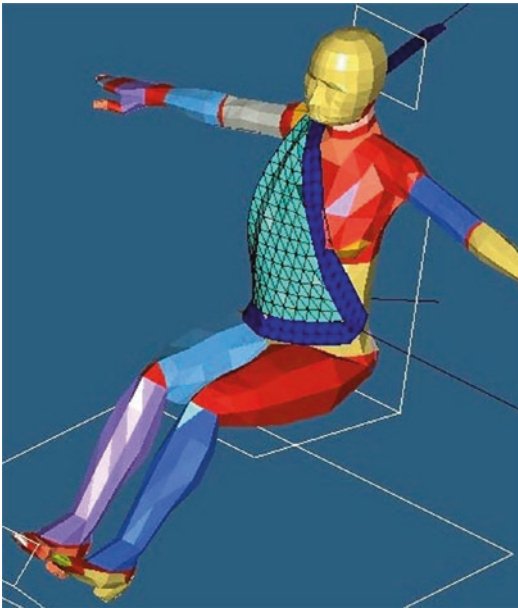
The lap belt should be placed under the gravid abdomen, snugly over the thighs, with the shoulder harness off to the side of the uterus, between the breasts, and over the midline of the clavicle [107]. Seat belts placed directly over the uterus can cause fetal injury [108]. The three-point and the four-point belts are superior in protecting the pregnant occupant by reducing the movement toward the farside door and eliminating the head-strike potential. However, it results in some force to the abdomen, increasing the risk of fetal injury. This is an acceptable trade-off, given that the most critical factor in saving the fetus' life is keeping the mother alive. The four-point belt is better than the three-point belt concerning abdominal loading because some of the overall load is applied through the mother's neck. Therefore, less is applied to the abdomen to restrain her for the same crash speed. The belt

**Fig. 25.11** Four basic restraint systems used in automotive vehicles. (a) A *two-point belt* attaches at its two endpoints. (b) A “sash” or *shoulder harness* is a strap that goes diagonally over the vehicle occupant’s outboard shoulder and is buckled inboard of their lap. (c) A *three-point belt* is a Y-shaped arrangement, similar to the separate lap and sash belts, but unitized. Like the separate lap-and-sash belt, in a collision, the three-point belt spreads out the energy of the moving body over the chest, pelvis, and shoulders. (d) *Lap belt with a double shoulder harness* is an improved three-point belt that further spreads out the energy of the moving body over a larger body area



**Fig. 25.12** Simulations at 35 kph showing uterine compression for the correctly (a) and incorrectly (b) positioned lap belt, causing uterine fundal compression. (Modified and reproduced with permission from [104])





**Fig. 25.13** Advanced restraint (mesh webbing) for the pregnant occupant added to a standard three-point belt for maximum fetal protection. (Reproduced with permission from [104])

contact loads through the neck were below published injury thresholds [96]. Overall, the results indicate for all frontal and side impacts that, it is safest for the pregnant occupant to ride in the passenger seat while wearing a three-point belt or four-point belt if possible and utilizing the frontal airbag when appropriate [93].

Additional improvements lead to seat belts with larger areas for better impact absorption, further minimizing maternal and fetal injury. One includes a *mesh webbing* over the entire abdomen proved to be the best protective measure for the fetus. Another is the seat belt airbag (Fig. 25.13). The shoulder belt contacts the pregnant woman's neck in the third trimester of pregnancy while sitting in the rear seat of a sedan vehicle. Drivers and front-seat passengers can adjust the position of seat belt shoulder anchorage to adequately fit the belt path, unlike the passenger in the rear seats [109]. Seat belt-neck contact occurs in pregnant women of lower height. Small stature can become a risk of poor seat belt fit [109].

### The Seat Belt Syndrome

Distinctive injuries caused by seat belts due to MVAs were coined *seat belt syndrome* [100].

Frank E. Rubovits, in 1964, first reported traumatic rupture with avulsion of the uterine musculature at the site of the seat belt impact (lap belt). This was attributed to the force of the belt at the anterior uterine wall being transmitted to the fetus, blasted then through the left uterine wall [89]. This was fatal to the fetus. The absence of a sign of shock or intraperitoneal bleeding precluded diagnosis for 2 days.

Injuries caused by the seat belt are most likely as follows [79]:

- Abdominal organ damage,
- Bowel rupture,
- Abdominal wall injuries,
- Ruptured liver,
- Blood vessel trauma,
- Chest trauma,
- Fractured sternum,
- Myocardial contusion,
- Spine fractures.

### Seat Belt Use Counseling

The correct seat belt position prevents potential harm to the mother and fetus. Improperly positioned restraints increase the risk of intra-abdominal injuries or uterine rupture at the collision [110]. In 1992, The American College of Obstetricians and Gynecologists (ACOG) recommended that all women receive seat belt counseling from prenatal care providers. Nevertheless, many pregnant women report uncertainty about the safety and use of seat belts during pregnancy [111] and a lack of information regarding proper seat belt use and its role in protecting the fetus [112]. A 2004 study reported that 45% wear their seat belts (both before and during their current pregnancy), even though 72.5% demonstrated the proper seat belt position [112]. Unfortunately, only 58% thought that seat belts would have a positive effect if they were in an MVA during pregnancy, 34% were unsure of the effect, and 8% thought the seat belt would cause them to get hurt [112]. When asked if a seat belt would help protect their baby in a crash, only 55.3% thought it would help, 10.7% said it would harm, and 34% were unsure [112]. The women who thought a seat belt would help protect them were significantly more likely to report always wearing a seat belt vs. the women who were unsure or thought

negatively of the seat belt (84.4% vs. 64.6%) [112]. Therefore, prenatal care providers should take the opportunity that prenatal visits provide to educate women on the importance of proper use of seat belts during pregnancy to protect both the mother and fetus [113], as well as clear up any misconceptions that a woman may have about seat belt use. A study from Hong Kong showed that 76.6% of pregnant women reported using a seat belt 6 months before pregnancy, but compliance was reduced as the pregnancy progressed. Seat belt use was reduced to 73.5% in the first trimester, 70.5% in the second trimester, and 67.1% in the third trimester. The most common reasons for not using a seat belt were: not useful (12.6%), causing discomfort (89.1%), and may harm the fetus (45%) [114].

Prenatal care provider counseling for seat belt use occurred in 48.7% of prenatal visits; women aged 20–29, nonwhite, Hispanic ethnicity, and less educated were the most likely to report being counseled on seat belt use; women who were 30 or older and had a greater than high school education were more likely to report always wearing seat belts in the last trimester; and on average, 2.3% reported being hurt in a “car accident” during pregnancy. Women <20 years old, of the black race, and less educated were the most likely to report being hurt in a crash during pregnancy. It is encouraging that black women are the most likely to report being counseled on seat belt use during pregnancy because they are more likely to report being hurt in a crash.

All women should be counseled on the importance of seat belt use and how to properly wear a seat belt during pregnancy regardless of age, race, ethnicity, or education.

During the last decades, the use of seat belts has increased from <50% [112] to >90% [115, 116]. Unfortunately, seat belt users decreased from 94.5% to 86.7% among women after becoming pregnant [81]. In Japan (since 2008, seat belt use has become legally mandatory for rear seat passengers), pregnant women who reported preferring the rear seat increased from

16.7% to 23.8% [81]. However, the prevalence of pregnant women who always fastened their seat belt among those preferring the rear seat was 78.4%, significantly lower than those preferring the front seat, 89.2% [81]. Significant factors influencing rear seat belt use during pregnancy are acquiring information on how to wear a seat belt correctly during pregnancy and age >30 years [117].

The percentages of counseled women were 48.7% in 22 PRAMS states, 53% in 14 PRAMS states during 1997 and 1998 [118], and 48% in 19 PRAMS states in 2000 [113].

The issue with seat belt counseling during pregnancy is that some women forget some topics discussed. Up to 73% did not recall receiving advice on seat belt use even though they received brief counseling from a clinician and a pamphlet on seat belt use during pregnancy during their initial visit [119]. The new teaching methods, such as audiovisual aids, mannequins, or having women demonstrate proper seat belt use to the healthcare provider, may increase knowledge retention [119]. The women who received seat belt use instructions were more likely to use restraints and correctly identify restraint positions than those who received no information [120, 121].

### Belted and Unbelted Pregnant Women

Pregnant women in crashes where mothers wore seat belts had no significantly increased risk for adverse fetal outcomes than pregnant women not in crashes. Pregnant women who did not wear seat belts during a crash were more likely to have [78, 122, 123]:

- Low birth weight infant,
- Birth within 48 h,
- Excessive maternal bleeding,
- Prematurity,
- 3× higher incidence of fetal death.

The belt use effectively reduces morbidity and mortality for the mother and the fetus [91, 122, 124]. Belted pregnant women in crashes do not have an increased risk for adverse fetal outcomes than the general pregnant population [19]. The odds of adverse fetal outcomes, including fetal loss, preterm delivery, placental abruption, and uterine laceration after an MVA, were 4.5 times



higher among not properly restrained than properly restrained women at the time of the crash [125]. Lack of seat belt use has been associated with a low birth weight with an increased risk of delivery within 48 h of the crash [122]. There is no increased risk of immediate delivery. Unbelted pregnant women were 2.8× more likely to experience fetal death than belted pregnant women in crashes [78]. However, some did not find a statistically significant increase in the risk of fetal death associated with a lack of seat belt use [122]. A population-based study published over 40 years ago reported that lap belt use reduced maternal injury and death. However, there was no association with fetal loss [124]. Most fetal deaths (51%) were linked to crashes during the first trimester, even though all deaths occurred during the second and third trimesters. This may result from the fact that first-trimester crashes have up to 36 weeks to result in fetal death, whereas the other trimesters have correspondingly less time to do so. Essentially, there was a longer exposure period of gestation in which fetal deaths could occur, whether those fetal deaths were related to the crash. Another possibility is that the last trimester may be offset by an increased likelihood of these infants being born through trauma- or physician-induced labor, which may have resulted in deaths not recorded in the fetal death file. Finally, the finding may suggest that the first trimester represents a sensitive period of fetal development and vulnerability to crashes but that fetal deaths do not occur (or go unnoticed) until a few weeks later in development. Also, there is an increased risk of fetal death for unbelted crashes during the later weeks of gestation. When comparing gestational age and the time of fetal death, the unbelted group had sharp increases in fetal deaths during 31–38 weeks' gestation. This may indicate a period of increased vulnerability to fetal death from MVA among unbelted drivers. One might believe that this increase results from more crashes during the third trimester. However, all births involving unbelted MVA showed that only 25% of crashes occurred during the third trimester, the lowest percentage of any trimester. On the other hand, 55% of fetal deaths among the unbelted group were linked to third-trimester crashes. Therefore, this pattern probably results from something

different than increased crash risk. These findings have implications for health providers and researchers involved with crash dummy development. For instance, crash dummy testing has mainly focused on the 28–30-week gestational age period for designing the physiological characteristics of a pregnant woman and the fetus [92, 107]. It is important to design dummies representing a few weeks later in gestation to more appropriately target the population at the greatest risk for fetal death. Despite substantial research on seat belts' protective value, many women still do not wear them during pregnancy. Previously, the leading reasons for the lack of seat belt use during pregnancy included forgetting, discomfort or inconvenience, no seat belt available, and fear that seat belts may cause injury to the fetus or mother [126]. Some countries even exempt pregnant women from seat belt laws, which may promulgate misconceptions about seat belt use during pregnancy. Many women are unaware of seat belts' correct usage and positioning [121].

Factors associated with low seat belt compliance—younger age, lower education, lower socioeconomic status, seating location (passengers), and longer annual distance traveled—are also important during pregnancy [127, 128]. Before seat belts became mandatory in Japan, seat belt use during pregnancy was reduced for drivers and front-seat passengers compared with seat belt use before pregnancy [129]. This trend is contrary to the finding in California that seat belt compliance significantly increased during pregnancy (79% before pregnancy vs. 86% during pregnancy) [119]. A study in New Mexico, where seat belt use was generally low, found that seat belt use increased from 27 to 42% during pregnancy [126]. If concerns associated with the gestation period dissuade maternal seat belt use, then the gestation period would be a major determinant for nonrestraint use during pregnancy. However, a study from the USA reported that trimester status has little effect on seat belt use [19].

Pregnant women who reported receiving educational information were more likely to wear seat belts and do so correctly [116, 120, 121]. Daily car users were less likely to wear seat belts despite their longer exposure to the risk of traffic injuries. This suggests that frequent car use may lower risk perception [127, 128]. Recommendations support

## IF YOU'RE PREGNANT SEAT BELT RECOMMENDATIONS FOR DRIVERS AND PASSENGERS

### I'M PREGNANT. SHOULD I WEAR A SEAT BELT?

**YES**—doctors recommend it. Buckling up through all stages of your pregnancy is the **single most effective** action you can take to protect yourself and your unborn child in a crash.

**NEVER**  
drive or ride in a car  
without **buckling up** first!

### WHAT'S THE RIGHT WAY TO WEAR MY SEAT BELT?



### SHOULD I ADJUST MY SEAT?



\* If you need additional room, consider adjusting the steering wheel or having someone else drive, if possible.  
\*\* If you're a passenger, move your seat back as far as possible.



**Fig. 25.14** Leaflet about the proper position of the seat belt in pregnancy (US Department of Transportation, National Highway Traffic Safety Administration) *If*

*You're Pregnant: Seat Belt Recommendations For Drivers and Passengers (tmcaz.com)*

using a three-point belt for pregnant women [102]. The lap belt should be placed as low as possible, beneath the bulge of the uterus, and the shoulder

belt should lie to the side of the uterus and run between the breasts and over the midportion of the clavicle (Fig. 25.14).

## The Airbag

Simulations indicate that for all frontal impacts, it is safest for the pregnant occupant to ride in the passenger seat while wearing a three-point belt and utilizing the frontal airbag when appropriate [94].

The airbag is a standard passive safety system for vehicles. In a crash, the airbag is opened using sensors within 30–50 ms. It is rapidly filled with gas, usually nitrogen, to softly await passengers' bodies and absorb the inertial force of the body. Airbags for drivers and passengers should protect against head and chest injuries in a frontal crash. Airbags work in combination with three-point belts for the full effect. In the collision of the head and upper body, the airbag must not constitute a solid barrier to maintain constant pressure. The body hitting the bag pushes gas filling through the exhaust openings from the airbag. To ensure the active airbag filling, at least two sensors are in the vehicle, the bumper and the divider between the engine parts and passenger space. A few milliseconds after impact, the sensor system transmits an electronic signal that activates the initial capsule with approximately 8 g of plastic explosives. The explosion lits the initial mixture in the generator gas, whose combustion releases nitrogen to fill the airbag. The airbag is, after being inflated and depreciated by the impact of the driver, blown out, and the whole cycle takes about 150 ms. The negative effect of opening the airbag and a loud burst of the strength of 140–160 dB should not threaten human hearing because the vehicle's impact on another vehicle or object creates a louder noise.

The biggest imperfection of airbags is their ability to activate when they are not expected. Except for failure in the system that may cause the airbag to open, there is a risk that the airbag opens in collisions when a vehicle has low speed, and the airbag is not needed to absorb the body's impact on the steering wheel. In such cases, due to low speed, the body does not come into contact with the vehicle's interior because of its small

inertia forces, but it reinforces the seat belt in the vehicle seat. If the airbag is activated, it can cause head and chest injuries, which would not emerge if the airbag is not activated.

Such injuries are hazardous because they can cause the death of the fetus. This is solved with airbags opening at certain vehicle speeds or specific vehicle body deformation. Some small studies did not find significant maternal or fetal injuries with airbag activation during slow-speed collisions [130]. In contrast, others found a fetal death due to skull fractures with intracranial bleeding [131] or placental abruption [132]. Conclusions are not firm because, sometimes, additional risk factors, for example, intracranial bleeding, such as maternal anticonvulsant therapy, can increase fetal oxidative degradation of vitamin K, resulting in deficiency and possibly causing neonatal bleeding [131].

Measurements on the dummies in crash tests showed significantly less stress in the critical part of the cervical vertebrae and minor injuries when using a large “bull-size” airbag. Newer-generation airbags are programmed to strain safety belts with a pyrotechnic strainer that works with the new generation of airbags. These bags can bend from top to bottom and sideways, allowing regular distribution of tensions in the chest and having a specially calibrated valve that regulates the throughput power and exhaust of gas. Combined protection proved much more successful than previous methods, so chest injuries are 70% less.

Airbags should not be disabled during pregnancy [107, 108].

### 25.3.3.5 Pelvic Fractures

For acute pubic symphysis diastasis/rupture, see Sect. 10.1.9.1.

#### Incidence

The commonest severe fracture reported in pregnancy is a pelvic fracture. Fractures of the extremities, ribs, and vertebrae do not necessarily affect pregnancy. The most common pelvic fractures are through the anterior half of the pelvic

ring, usually the horizontal pubic rami [133]. The most common is a coccyx fracture, which occurs when a pregnant patient falls on her buttocks.

### Pathophysiology

Pelvic fractures commonly result in retroperitoneal hematomas. The sudden increase of intra-abdominal pressure leads to the rupture of the congested, engorged pelvic venous plexus, fed by the utero-ovarian and infundibulopelvic vessels, into the retroperitoneum [120]. Traumatic retroperitoneal bleeding is often associated with consumptive coagulopathy, with a high incidence of fetal death [134]. Massive substitution of blood products is often required, and a nonoperative approach is initially usually pursued.

### Clinical Presentation

The most consistent finding of pubic symphysis diastasis is a pain in the symphyseal region that radiates to the lower back and thighs and is exacerbated by leg movement. The pain increases when manual pressure is applied to the pelvis in a laterolateral and anteroposterior direction. Other symptoms include tenderness, instability, and allodynia at and around the joint site. In addition, many women will have difficulty walking. The gait is waddling or painful, with the inability to stand or walk.

### Diagnosis

See Sect. 25.3.7.2.

### Treatment

See section “[Pelvic Fracture Treatment](#)”.

### Obstetric Considerations

See section “[Maternal Pelvic Fractures](#)”.

### Prognosis

Overall, the outcome of patients with pelvic fractures in pregnancy from blunt trauma correlates with the severity of associated injuries and physiological derangement on admission rather than with characteristics, or the type, of pelvic fracture. Pelvic fractures in young patients require transmitting significant amounts of kinetic energy. It is an index injury mandating a thor-

ough search for other occult visceral injuries. Fractures of the sacrococcygeal joint with ankylosis and encroachment on the capacity of the pelvic outlet may be of obstetric significance [135].

#### 25.3.3.6 Urinary Bladder Rupture

See Sect. 28.3.

#### 25.3.3.7 Traumatic Rectus Sheath Hematoma

See Sect. 26.4.

### 25.3.4 Falls

*Aborcement may happen by over much strearynge of the bodye in laborynge, daunsying or leaping, or by some fall or thruste agynst some wall or beatynge.*

(Thomas Raynalde, “The Byrthe of Mankynde,” 1542)

Falls accounted for more than half of classifiable reported maternal injuries during pregnancy, and about 3% of all mothers reported at least one fall. Falls are also the leading cause of nonfatal injury among women of childbearing age (15–44 years) in the USA, although they account for only 20% of nonfatal injuries among the general population [136]. Falls may be a more common mechanism of injury during pregnancy, particularly in the second and third trimesters, because of [137]:

- Weight gain,
- The shift of the center of gravity,
- Increased joint mobility.

Increased relaxin levels result in softer ligaments, cartilage, and cervix, allowing the tissues to spread during delivery. The pubis symphysis—cartilage joining the pubic bones—and sacroiliac joint, where the hips attach to the spine, become unstable during pregnancy to aid delivery.

Falls are more likely as the pregnancy progresses, with 43% occurring during the third trimester [138, 139]. Although extensive clinical

guidelines (*American Geriatrics Society, British Geriatrics Society*) exist for counseling about the importance of fall prevention in the elderly, clinical guidelines for counseling about fall prevention for pregnant women are limited to warnings against strenuous physical activities with high risk for falls, such as horseback riding and skiing. In the injury descriptions, falls during pregnancy most often occurred during normal daily activities.

## 25.3.5 Social and Domestic Violence

### 25.3.5.1 Introduction

There are two types of social violence: homicide and suicide. Such violence during pregnancy has been identified as a risk factor for homicide by an intimate partner [140]. Suicide may represent the only way out of repeated episodes of domestic violence [141]. An intimate partner or family member carries out domestic violence. Unwanted pregnancy, sometimes because of sexual abuse, may lead to suicide under social circumstances stigmatizing women who have a pregnancy out of wedlock. It is especially evident in societies where access to family planning is limited, and access to abortion is restricted. The neglect of the contribution of violent deaths to maternal mortality seems to be due to the misconception that homicide, suicide, and accidents occur only by chance during pregnancy. Because many women seek medical attention only when they become pregnant, healthcare providers of pregnant women play a crucial role in discriminating against abused women.

Deaths during pregnancy or the puerperium due to suicide, homicide, and accidents were initially excluded from maternal death and later classified as “pregnancy-related” by the Tenth Revision of the International Classification of Diseases. Understanding the relationship between violence in pregnancy and the adverse maternal outcome can have important clinical and public health implications for successful Safe Motherhood initiatives.

### 25.3.5.2 Incidence

With an unborn child’s safety in mind, women are more motivated to seek assistance and to speak more freely during pregnancy. The reported abuse rates vary significantly, 4–27.7% [142–145]. This reflects a genuine diversity in violence and definitions of abuse used. The prevalence of interpersonal violence during pregnancy ranged from approximately 2.0% in Australia, Cambodia, Denmark, and the Philippines to 13.5% in Uganda among ever-pregnant, ever-partnered women; half of the surveys estimated a prevalence of 3.9–8.7%. Prevalence appeared to be higher in African and Latin American countries than in European and Asian countries. In most settings, the prevalence was relatively constant in the younger age groups (15–35 years) and then declined slightly after age 35 [146]. As many as 20.6% of pregnant teenagers and 14.2% of pregnant adult women were physically abused during pregnancy [147]. Interpersonal violence has only been emphasized as an etiology of trauma during the past few decades. Sexual or physical abuse occurs in up to 17–32% of pregnancies, and 60–75% of those abused reported multiple episodes of abuse with (repeated) hospitalizations [30, 148, 149]. This scenario can be repeated in subsequent pregnancies [149]. Abuse often begins or escalates during pregnancy or the immediate postpartum period. Most often, the abuser is known to the patient, frequently a husband or partner. Initial maternal injuries include the head and neck in 42.2%. Injuries to the torso were identified in 21.5% during pregnancy vs. 8.7% during the puerperium. The leading physical injury was a contusion or superficial injury in 25.4% of patients [150].

### 25.3.5.3 Risk Factors

#### Age

Young women (<25 years) comprised 59% of maternal deaths due to injuries, whereas injuries constitute 47% of all maternal deaths in Maputo [151]. In Bangladesh, pregnant or puerperal women aged 15–19 years were nearly three times



more likely to die from injuries than nonpregnant and nonpuerperal women of the same age. They were also at a significantly higher risk than older women [152].

### Substance Abuse

There are strong associations between violence and substance abuse. Victims of violence are more likely to smoke, drink alcohol, and use illegal drugs before and during pregnancy [153, 154].

### Psychiatric Disorders

Important determinants of suicide risk include psychiatric disorders, such as major depressive disorder, panic disorder, generalized anxiety disorder, violence by partners, being unmarried, unemployment, and unintended pregnancy, which are the main reasons for suicide attempts [155].

### Violent Coitus

Hippocrates expressed a cause-and-effect relation between coitus and abortion. Pinard claimed that repeated intercourse predisposed to abortion more commonly in primigravidas than multigravidas. Borras added that the greater frequency of intercourse and generally smaller vaginas in primigravidas might be the cause. Bumm advised sexual continence during early pregnancy. Baisch recommended abstinence from coitus during the first and third trimesters. Meyer showed experimentally that repeated sexual intercourse disturbed the normal metabolic relations between the corpus luteum and the implanted ovum [63]. Others did not find any relation between coitus and (threatened) abortion, claiming abortion is coincidental. This second option is closer to the truth because otherwise, the incidence of abortion would be much higher. The only subgroup with a theoretically higher incidence of (threatened) abortions is couples practicing violent coitus when minor blunt abdominal trauma is possible. The unevidenced advice is: *“There is no evidence that sexual intercourse causes miscarriage. But it can be pragmatic to advise women*

*with threatened miscarriage to avoid intercourse until after the bleeding has completely resolved so if miscarriage does occur, the couple does not feel that they may have triggered or exacerbated events.”* The only paper reporting any evidence on the association between sexual intercourse and early pregnancy loss is a retrospective questionnaire study with many inadequacies (poor response rates, massive potential for selection and recall biases, post hoc recategorization of case and control groups, and insufficient acknowledgment of confounding factors) limiting the believability of its findings [156]. Violent coitus increases the possibility of sexual abuse and domestic violence that could cause abortion, not the coitus itself.

The risks include bleeding, pelvic inflammatory disease, placental abruption, venous air embolism, and uterine rupture. Sexual intercourse is not associated with vaginal bleeding in the first trimester. Dissimilarly, vaginal bleeding after sex in the second and third trimesters has been associated with placental abruption and antepartum hemorrhage related to increased frequency of intercourse [157]. One of the known risks of bleeding during cervix manipulation is placenta previa. Therefore, placenta previa could be the reason to avoid sexual intercourse during pregnancy.

Venous air embolism is a distinct risk of sex in pregnancy with an incidence of <1:1,000,000. Twenty-two cases were associated with sex, while 20 occurred during pregnancy or puerperium. Eighteen of 22 women died. While uncommon, this is a complication of sex during pregnancy with very high mortality. The women should be advised to avoid rough sex. A high-pressure gradient is created, particularly in the rear entry position, when the heart is positioned below the level of the distended vaginal vasculature [158].

#### 25.3.5.4 Clinical Presentation and Diagnosis

Domestic violence occurs in up to 25% of pregnant women [159, 160], while physicians detect

**Table 25.5** Warning signs of domestic abuse

|                                                                                                                                                                            |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| A mixture of old and new injuries                                                                                                                                          |
| Characteristic injuries (multiple soft tissue injuries, fingernail scratches, cigarette and rope burns, areas usually covered by clothes—breast, chest, abdomen, genitals) |
| History of prior domestic abuse                                                                                                                                            |
| The isolating behavior of the partner                                                                                                                                      |
| The behavior of the patient: depressed, poor eye contact, fearful, withdrawn                                                                                               |
| Pregnant patient: trauma to breast and abdomen; no prenatal care; unexplained spontaneous abortion, miscarriage, or spontaneous labor                                      |
| Family income <\$10,000/year                                                                                                                                               |

Reproduced with permission from [159]

only 4–10% [30]. Regardless of the apparent injury severity in blunt trauma, all pregnant women should be evaluated in a medical setting [5]. Patients should be screened for domestic violence and be familiar with the community resources for helping patients who experience domestic abuse [159]. The pregnant patient presenting with blunt trauma, not from traffic, should be examined for signs of older trauma leading to chronic violence. As with any trauma patient, the entire body should be examined, looking for hidden injuries under clothes, makeup, jewelry, or wigs. Injuries range from cuts, bruises, and black eyes to miscarriage, bony injuries, splenic and liver trauma, partial loss of hearing or vision, and scars from burn or knife wounds. Injuries to the breast, chest, and abdomen are more common in battered women, as is the presence of multiple old and current injuries. Defensive injuries are common. For example, fractures, dislocations, and contusions of the wrist and lower arms result from attempts to fend off blows to the chest or face. Injuries inconsistent with the patient’s explanation of the mechanism of injury should also raise suspicion of abuse. These injury patterns should raise concerns about abuse during evaluation in the emergency room (Table 25.5).

### 25.3.6 Obstetric Complications

The presence of blood at the vaginal introitus in a pregnant trauma patient should prompt the trauma and obstetric team to rule out placenta previa, placental abruption, placental tear, labor,

or even UR. Nonobstetric causes include urethral or bladder injury. If a nonobstetric cause is suspected, a urologist should evaluate the patient before a Foley catheter placement.

There are two principal mechanisms of obstetric trauma: direct injury and deceleration injury. Both types have specific obstetric trauma patterns, while some, such as traumatic placental abruption, are common.

#### 25.3.6.1 Traumatic Placental Abruption

##### Incidence

The incidence of traumatic placental abruption is approximately 5–6% [12, 65, 124, 161]. Clinically evident placental abruption occurs in up to 40–50% of severe blunt abdominal trauma and 1–6% of minor trauma with direct uterine trauma [12, 162–164]. Placental abruption is difficult to predict based on the severity of trauma [65]. The seat belt sign in pregnancy (Fig. 25.15) increases the risk of traumatic placental abruption and, to a lesser degree, fetal head injury and uterine rupture. A seat belt sign results in a 55× increased rate of placental abruption. The mean ISS of the seat belt sign



**Fig. 25.15** Seat belt sign in advanced pregnancy

group was significantly higher (19.3 vs. 9.13,  $p = 0.031$ ) [165]. Additional predisposing factors, such as cigarette smoking and cocaine use, increase the incidence of decidual necrosis. The placental abruption rate increases in preeclampsia, diabetes mellitus, multiple births, short umbilical cord, and velamentous cord insertion [166, 167].

*Retroplacental hemorrhage* differs from placental abruption, which is a clinical diagnosis. There is premature separation of the placenta from the maternal surface with decidual hemorrhage. A large retroplacental hematoma involving the central area and up to 40% of the maternal surface will cause fetal embarrassment. In contrast, smaller retroplacental hematomas may prove equally embarrassing in pregnancies where the maternal blood supply is diminished, as in maternal hemorrhagic shock. There is an association between premature delivery, PROM, and peripheral placental bleeding [168].

### Pathophysiology

The mechanism of placental abruption resulting from trauma is based on the fundamental differences in tissue characteristics between the uterus and the placenta. The uterus consists of a signifi-

cant proportion of elastic fibers, whereas the placenta is mainly devoid of elastic fibers. Thus, its plasticity allows deformation when an external deforming force is applied to the uterus. At the same time, the placenta cannot undergo similar deformation, and a shearing effect is created at the uteroplacental interface. The concomitant increases in amniotic fluid pressures propagate this shearing effect, further separating the placenta from the underlying decidua (Fig. 25.16). Experiments on pregnant baboons subjected to decelerative forces ( $\sim 20G$ ) typical of MVAs produce very high intrauterine pressures ( $\sim 550$  mmHg) [169].

Because most blunt abdominal trauma occurs to the anterior uterine wall, one would expect that if the separation mechanism was just the displacement from the striking object, the risk of placental abruption would be greater when the placental location is anterior. However, the pathophysiological mechanism of separation described does not explain the finding that an anterior placental location does not appear to be a risk factor for placental abruption resulting from trauma [65]. Two alternative possibilities should be considered. Firstly, the mass within the amniotic fluid (i.e., the fetus) can strike the



**Fig. 25.16** Acute deceleration injury occurs when the elastic uterus meets the steering wheel. As the uterus stretches, the inelastic placenta shears from the decidua basalis. (Modified and reproduced with permission from [137])

placenta in any location and thus create a potential shear or pull the placenta by transmitting forces via the umbilical cord. A second possibility that could explain the lack of importance of placental location on the likelihood of placental abruption is that traumatic deformation may set up a fluid wave within the uterus. A force striking the anterior uterine wall would cause elongation and narrowing of the uterus as the contained amniotic fluid is noncompressible. The fluid wave would then “rebound” and expand horizontally, causing the shortening and widening of the uterus. Again, because of the fundamental tissue differences between the uterus and placenta, a shearing effect of this interface could occur independently of placental location [44, 70]. The risk of placental abruption is independent of placental location.

The vena cava compression resulted in placental abruption in animal experiments during the 1950s [170, 171]. Therefore, when placental abruption does not occur immediately after trauma, it may result from placing an injured patient in the supine position [42].

Placental abruption is more likely if the vehicle speed exceeds 50 km/h [172].

Pregnant trauma patients can consume legal and illegal substances that increase the incidence of placental abruption. Alcohol easily crosses the placenta and accumulates in the fetus and amniotic fluid [173]. Alcohol causes vasoconstriction in the placenta and umbilical cord [173]. No safe amount of alcohol consumption during pregnancy has been determined. Cocaine use also causes vasoconstriction in the placenta. Although the relationship between placental abruption and cocaine use is confounded by other risk factors, including drug and tobacco use and lack of prenatal care, cocaine use is an independent risk factor [174]. Amphetamine use is also associated with placental abruption [175].

### Clinical Presentation

Traumatic placental abruption may occur even when there are few other signs of trauma. It almost invariably results in the termination of pregnancy within 48 h of trauma [133, 176]. If the area of placental separation is large enough to compromise fetal oxygenation, labor or fetal

death will occur within 48 h. If death or labor does not occur within 48 h, harm to the fetus from the placental separation is unlikely [176].

Clinical findings may include vaginal bleeding, abdominal cramps, uterine tenderness, amniotic fluid leakage, and maternal hypovolemia out of proportion to visible bleeding. Only 35% of clinically significant placental abruptions had vaginal bleeding [55]. The remaining hematomas are confined to the uterus and do not manifest as vaginal bleeding. Up to 2 L of blood can accumulate in the uterus, which can cause maternal shock. However, the shock in patients with placental abruption is frequently not proportional to the observed blood loss and results from profound hypovolemia from additional injuries. In a patient with intrauterine bleeding, the uterus may be larger than normal for gestational age.

Principal maternal complications associated with placental abruption are (1) hemorrhagic shock resulting from acute blood loss with contraction of the intravascular compartment; (2) generalized coagulopathy from active consumption of clotting factors and consequent secondary fibrinolysis; (3) ischemic necrosis of distant organs, most frequently kidneys and the anterior pituitary gland; and (4) preterm PROM resulting from decidual hemorrhage.

### Diagnosis

Coagulation tests, such as PT and partial thromboplastin time, are indicators of DIC; >50% of clotting factors must be consumed before these test results become abnormal. Fibrinogen levels are sensitive indicators of DIC on serial testing. A fibrinogen concentration <200 mg/dL in a pregnant patient is abnormal. Clinical evidence of bleeding may appear when the value is <100 mg/dL. The platelet count decreases in concert with fibrinogen levels, but mostly, a greater decrease in the fibrinogen level than platelet count is present. The most sensitive laboratory test for the diagnosis of coagulopathy related to abruption may be the determination of fibrin–fibrinogen degradation products by various techniques, including D-dimer assays [177]. Despite being frequently elevated in placental abruption, most studies failed to demonstrate clinical usefulness as a screening test [177, 178].

Placental abruption is frequent with fetomaternal hemorrhage (FMH). However, screening for fetal blood cells in the maternal circulation with Kleihauer-Betke (KB) tests has a low specificity and is not recommended [15, 108, 179].

Diagnostic imaging modalities are described in Sect. 25.3.7.

### Treatment

Fetal compromise is present in over 60% of placental abruptions with a live fetus, and an immediate CS is indicated. The treatment of small abruptions depends on the vitality of the fetus. Vaginal delivery after nontraumatic placental abruption with intrauterine fetal death is safe and feasible when intensive medical resources are available [180]. Immediate rupture of the membranes is the key to successful delivery after fetal death [181]. A sharp curette or percutaneous transhepatic cholangiographic needle could be used to manually rupture the membranes while avoiding injury to the uterine cervix [181].

### Prognosis

Over 70% of fetal losses following blunt abdominal trauma result from placental abruption [43, 44, 70, 163, 182]. The overall fetal mortality with placental abruption is 54% [22]. If maternal shock occurs, fetal mortality approaches 80%. Infants born after placental abruption are generally significantly smaller for gestation than controls. For comparison, perinatal mortality following abruption in the general pregnant population is 50%, related to the strong association with PTL, and, paradoxically, is higher for singleton than for multiple births [167]. There are no studies on pregnancies after traumatic placental abruption.

#### 25.3.6.2 Placental Tear

##### History and Incidence

Traumatic laceration (rupture, fracture) of the placenta following blunt abdominal trauma is more infrequent than placental abruption. The

first published case was by VanSante in 1942, in which blunt trauma to the maternal abdomen resulted from a falloff a stepladder, followed by the spontaneous delivery of a stillborn. A placenta had a clean laceration through the fetal and the maternal surface in the area of the insertion of the umbilical cord [183]. In 1969, Peyser and Toaff reported a case following an MVA in which a radial tear involved the whole thickness of the placenta; the fetus subsequently bled to death *in utero* [184].

### Pathophysiology

There are two mechanisms of placental injury depending on the location of the placenta. The uterus, umbilical cord, and fetus were intact in all published cases [185].

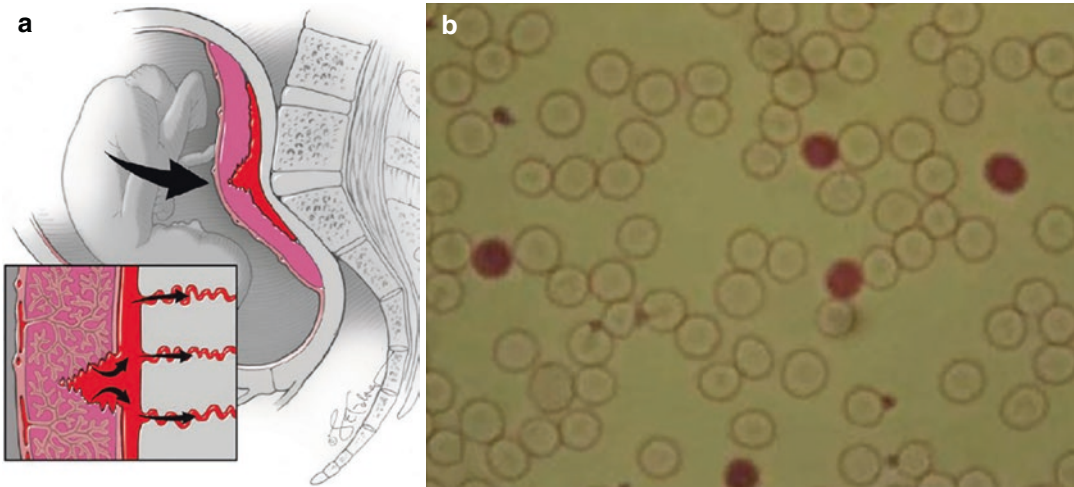
#### Countercoup Mechanism

With posterior placental implantation during deceleration, a countercoup mechanism is similar to closed-head injuries. Although the initial decelerative force is applied to the anterior abdominal and uterine walls, the incompressible amniotic fluid immediately anterior to the fetus would have retarded its forward movement. The sudden anterior force to the uterus momentarily causes the posterior uterine wall and the placenta to move away from the fetus, resulting in a “vacuum” between the fetus and the posterior wall. The posterior wall would have stopped moving when the anterior decelerative force was no longer applied to the uterus. The vacuum would have caused the fetus to be projected against the placenta on the posterior uterine wall. In this situation, the amniotic fluid, instead of acting as a buffer for the fetus, operates as a vehicle for fetal movement, allowing sufficient mobility for a countercoup injury of the placenta. This is analogous to the injury of the occipital region of the brain following a frontal blow when the cerebrospinal fluid acts as the vehicle for the countercoup movement of the brain.

#### Direct Placental Injury

With the anterior placental position, the initial decelerative force to the anterior uterine wall causes the fetus to be propelled forward. The





**Fig. 25.17** (a) Mechanism of placental tear or "fracture" caused by a deformation-reformation injury. Placental abruption is seen as blood collecting in the retroplacental space. (*Inset*) From here, blood can be forced into placental bed venules and enter maternal circulation. (b) Such

fetomaternal hemorrhage may be identified with Kleihauer-Betke testing. Peripheral smear of maternal blood. The dark cells constituted 4.5% of red blood cells are fetal in origin, whereas the empty cells are maternal. (Reproduced with permission from [137])

amniotic fluid, though incompressible, allows the fetus to travel forward with sufficient momentum to apply a sudden force to the surface of the placenta implanted on the anterior uterine wall, causing a "bursting" or irregular laceration of the fetal surface of the placenta (Fig. 25.17). Additional compression forces from an improperly positioned seat belt over the uterus increase the likelihood of placental tears [186]. Also, this mechanism increases the likelihood of uterine lacerations or UT (Fig. 25.18).

### Diagnosis

Diagnosis is made during emergent CS for fetal distress. With maternal hemodynamic stability, contrast-enhanced abdominal CT can reveal placental tears (Fig. 25.18). This is confirmed by placental examination after CS (Fig. 25.19).

### Prognosis

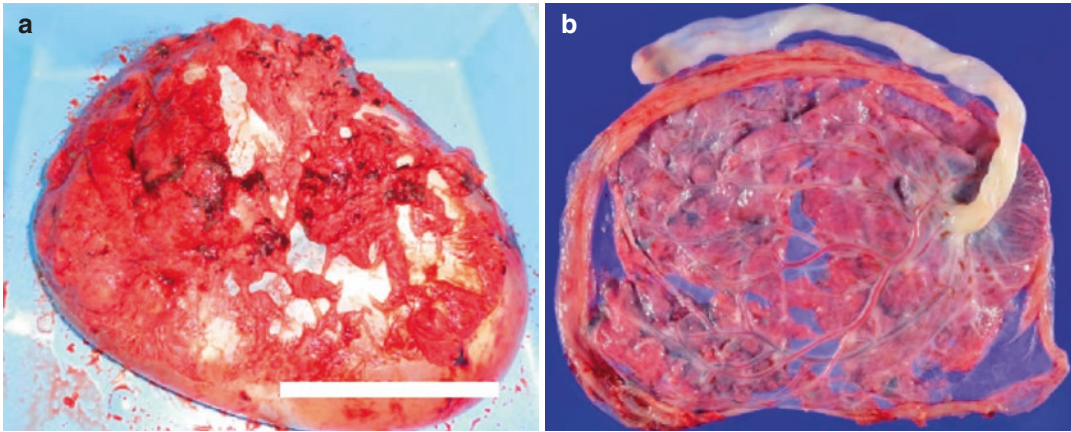
Fetal distress is an indication of emergent CS which increases fetal survival. The fetal mortality was high [183, 184]. Diagnostic workup for maternal or fetal injuries can define placental tears but delay in delivery results in fetal death [186].

### 25.3.6.3 Preterm Labor

See Chap. 4.



**Fig. 25.18** Contrast-enhanced abdominopelvic CT shows placental damage over the seat belt-compressed area with a well-circumscribed low-density area (white arrows). (Reproduced with permission from [186] under the CC Attribution License)



**Fig. 25.19** Traumatic placental rupture. (a) Maternal aspect just after *en caul* delivery. (b) The fetal aspect indicates placental lacerations. (Reproduced with permission from [186] under the CC Attribution License)

#### 25.3.6.4 Traumatic Uterine Rupture

See Chap. 10.

#### 25.3.6.5 Fetal-Maternal Hemorrhage

##### Incidence and Risk Factors

FMH or transplacental hemorrhage is a physiological transplacental passage of low fetal blood volume (fetal cells) into the maternal circulation. Therefore, it remains clinically insignificant and undetected. *Severe* FMH is a fetal blood loss >30 ml [187]. The estimated incidence of all-cause clinically significant FMH is 1/3000–1/10,000 women [187]. However, there is a high number of cases that remain unreported [188]. The reported incidence is 8–30% of traumatized pregnant women, compared to 2–8% of nontraumatized mothers, and the volume of transfused blood is also greater in injured women [55, 65, 70, 189]. Anterior placental location and uterine tenderness are associated with an increased risk of FMH. More important for determining the severity is the time frame in which blood is hemorrhaged and fetal and potential maternal mechanisms to counteract cardiovascular distress. In this context, gestational age might also play an important role [190].

Neither the severity of maternal injury nor the presence of uterine activity is predictive of FMH [12, 44, 65].

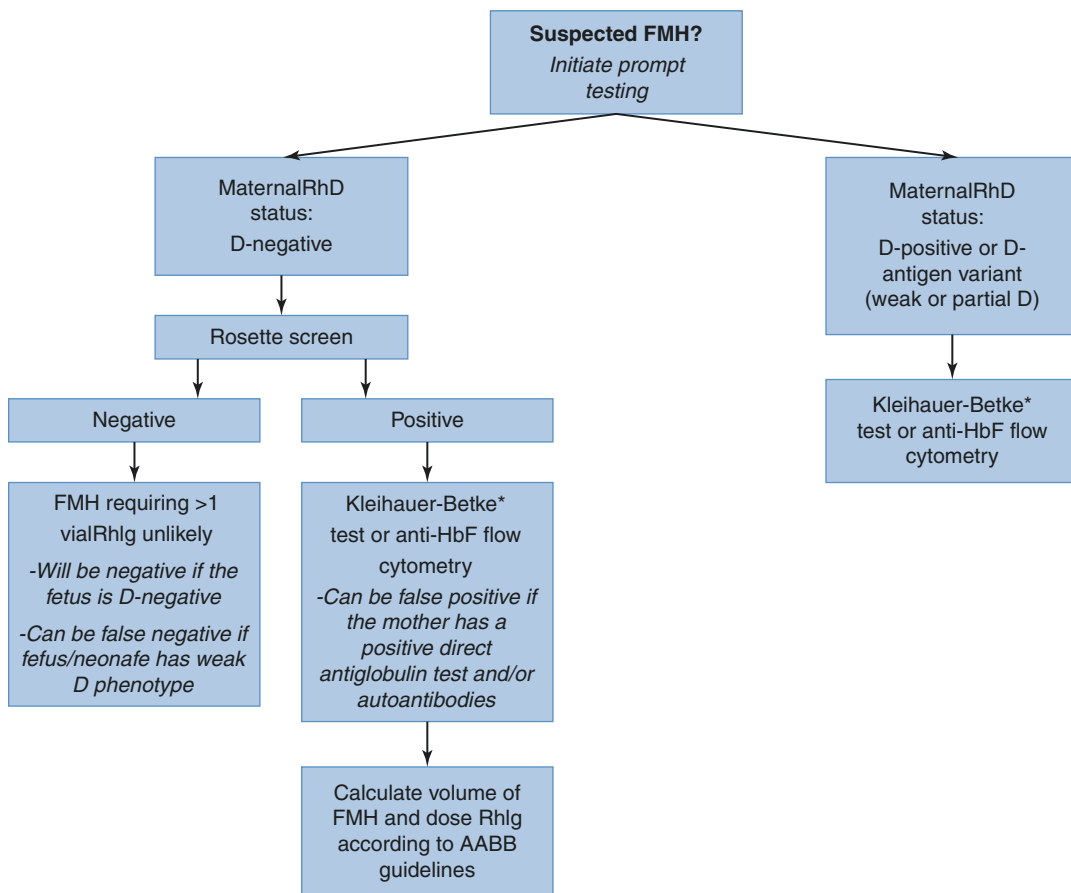
##### Clinical Presentation

Due to its rarity, even the experienced clinician will seldom encounter FMH. Therefore, it is crucial to detect the symptoms and signs of potential FMH early to take appropriate action to prevent further damage to the fetus and mother. Symptoms include neonatal anemia, followed by decreased or absent fetal movement and stillbirth. Also, potential signs are hydrops fetalis, pathological CTG pattern, and intrauterine growth restriction [187].

##### Diagnosis

When FMH is suspected, detecting fetal cells in the maternal bloodstream is necessary for confirmation.

With the *Kleihauer-Betke test*, fetal red blood cells containing fetal hemoglobin are identified by erythrosine staining; maternal red blood cells remain unstained (ghost cells). It is a semiquantitative test, an acid elution assay that may alert the obstetrician to a severe hazard to the fetus, even in Rh+ women. Before flow cytometry, the KB test was considered for every woman regardless of their Rh status to determine the Rh immune globulin dose necessary to be administered to women who are Rh– and suffered a massive transfusion [12, 43, 44, 55, 65, 189]. However, a positive test alone did not necessarily indicate FMH in low-risk pregnant trauma patients [179]. The positive KB test is present in 8–30.6%, indicating FMH [12, 55, 189]. These differences in the FMH rate are likely due to different inclusion



**Fig. 25.20** Suggested algorithm to detect fetomaternal hemorrhage. \*In case of known maternal elevation of fetal hemoglobin (i.e., HPFH, HPFH/sickle cell trait,

b-thalassemia), proceed to either anti-HbF or anti-D flow cytometry. *FMH* fetomaternal hemorrhage. (Reproduced with permission from [191])

criteria (noncatastrophic vs. catastrophic trauma) [149]. The KB test does not predict early or delayed complications after repeated blunt abdominal trauma. However, it should be performed in all D-negative trauma patients.

Using the *Rosette test*, a maternal blood sample is incubated with Rho(D) immune globulin, which will bind to any fetal Rh-positive *red blood cells* if present. Upon adding enzyme-treated cDE indicator cells, Rh-positive fetal blood causes rosetting, which is seen by *light microscopy*. The rosette screen is a highly sensitive method to qualitatively detect 10 ml or more of fetal whole blood, or 0.2% fetal cells (volume/volume), in the maternal circulation. In a positive test, it is recommended that a *KB test* or flow cytometry should be performed to confirm and quantify any positive rosette tests [191].

*Flow cytometry* using monoclonal antibodies directed against HbF has some important advantages over the KB test in the quantitation of FMH: (1) cytometric methods can accurately distinguish adult F-cells from fetal RBCs; (2) flow cytometry rapidly analyzes a greater number of cells ( $\geq 50,000$ ), improving quantitative accuracy; (3) as flow cytometry is automated, it has greater reproducibility [191].

*Flow cytometry is the method of choice for the estimation of FMH.*  
(British Committee for Standards in Haematology [192])

A suspected FMH requires immediate detection (Fig. 25.20).

### Treatment

Both mother and fetus should be treated. The volume of fetal blood loss after trauma varies between 5 and 40 ml, representing up to 34% of fetal blood volume. As little as 1 ml of Rh+ blood can sensitize 70% of Rh– women [189, 193]. Therefore, all Rh– mothers who present with a history of abdominal trauma should receive a prophylactic dose of Rh immune globulin. In Rh– pregnant women, administration of Rho(D) immune globulin is unnecessary after minor, superficial injury confined to an extremity. After any other trauma, the immune globulin should be administered within 72 h to all Rh– women, including those at less than 12 weeks of gestation and with minimal injuries [108]. The KB test can be helpful in Rh– mothers to roughly quantify the volume of FMH. All Rh– patients with a positive test should be treated with Rh-immune globulin (300 µg initially, and a positive test should be repeated in 24–48 h to investigate continuing FMH). One dose (300 µg) of the immune globulin is sufficient in 90% of cases of FMH because most FMHs are <30 ml of blood [108]. An additional dose of 300 µg for every 30 ml of estimated FMH is administered to reduce the risk of isoimmunization. Therefore, the KB test is unnecessary [40, 108, 178, 194] unless an FMH must be quantified for accurate dosing of the immune globulin [15, 108].

Severe FMH detected in a vital fetus with cardiovascular distress includes two treatment options: delivery or prolonging pregnancy (Fig. 25.21). The latter includes intrauterine blood transfusion (IUT) and the application of steroids at a gestational age of 23 weeks and 5/7 days for lung maturation. Fetal transfusions are given until 35 weeks of gestation, with delivery anticipated at 37–38 weeks. If the pregnancy is near-term, emergency delivery and immediate blood transfusion are the treatment of choice, particularly if transferring to a unit with an IUT facility would be time-consuming. IUT treatment after 32 weeks of gestation might be safer than procedures performed in early gestation and may prolong pregnancy until safe term and improve outcome [195, 196]. However, every IUT carries a risk of procedure-related asphyxia, especially in a compromised fetus.

### Prognosis

The mechanism of trauma-induced preterm labor is described in Sect. 4.3.3.3. Fetal complications of FMH include fetal/neonatal anemia, fetal tachycardia/arrhythmia, and intrauterine fetal death due to hypovolemia and cardiac failure [12]. Therefore, investigating unexplained fetal death should include maternal KB testing [197]. KB test on vaginal blood from antepartum hemorrhage can identify a fetal bleed [198, 199].

A Kleihauer-Betke test does not predict fetal outcome [15, 22, 40, 65, 108, 200].

The incidence of FMH adverse outcomes is 31–46%, mostly perinatal death. Morbidity is mostly neurological in the form of periventricular leukomalacia [201, 202].

Maternal complications of FMH include rhesus (Rh) sensitization in the mother. Although the incidence of FMH is 4× higher in pregnant women with trauma than in pregnant women without trauma, and the amount of FMH is 4× higher in trauma cases, these two patient groups have similar outcomes [65].

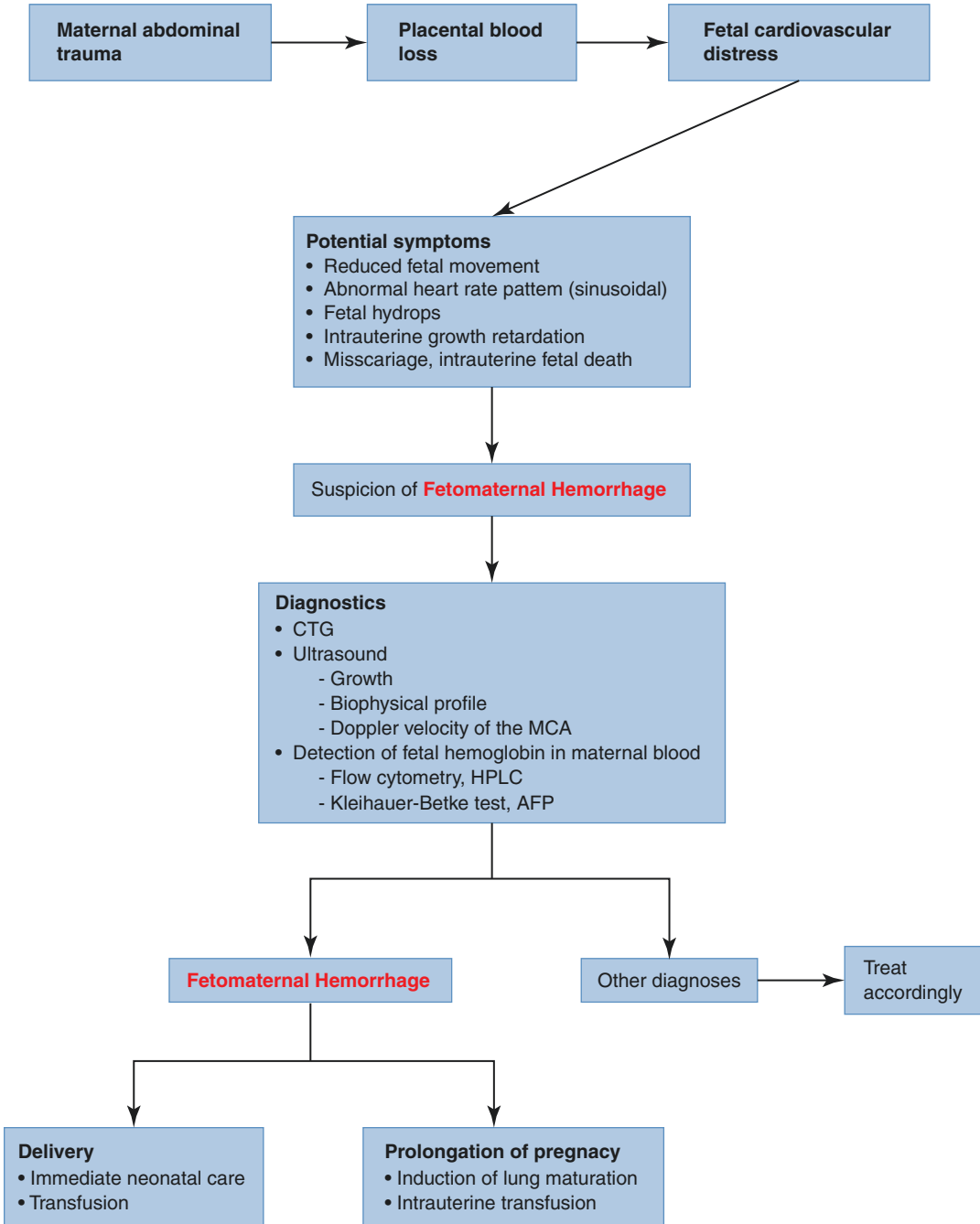
#### 25.3.6.6 Amniotic Fluid Embolism

##### Historical Considerations

Ricardo Meyer, in 1926, first described amniotic fluid embolism (AFE) [203], although Edward P. Davis, in 1905, described clinical presentations of sudden pulmonary thromboses similar to AFE [204]. Even in 1825, Matthew Baillies described macropathology that resembled AFE [205]. Paul E. Steiner, in 1941, established AFE as a clinical entity by discovering fetal mucins and squamous epithelial cells in maternal pulmonary vessels [206]. Cornelius Olcott et al., in 1973, published the first case of AFE after blunt abdominal trauma in pregnancy [207].

##### Incidence

The overall incidence in older studies, probably underreported due to unexplained deaths after an autopsy, was 1/8000–1/80,000 live births [206, 208]. The current incidence is 1.2–



**Fig. 25.21** Management after diagnosed fetomaternal hemorrhage from maternal blunt abdominal trauma. (Reproduced with permission from [190])

7.7/100,000 pregnancies [209, 210]. Five cases after maternal trauma were published, with the additional case after the fundal pressure maneuver (Kristeller maneuver) [207, 211–215]. Abdominal trauma represented one case

from 272 collected until 1979 [216]. The traumatic AFE is probably underreported, and some cases of post-traumatic hemorrhage were attributed to traumatic hemorrhage and DIC, not AFE.



**Table 25.6** Risk factors for amniotic fluid embolism [210, 220–222]

| Pregnancy-related             | Obstetric/traumatic                   |
|-------------------------------|---------------------------------------|
| Maternal age >35 years        | Cesarean delivery                     |
| Chronic hypertension          | Labor induction                       |
| Multiple pregnancy            | Instrumental vaginal delivery         |
| Gestational diabetes mellitus | Therapeutic abortion                  |
| Placenta previa               | Amniocentesis                         |
| Placental abruption           | Gestational age <37 weeks at delivery |
| Polyhydramnios                | <i>Cervical or uterine trauma</i>     |
| Eclampsia                     |                                       |
| Opaque amniotic fluid         |                                       |

### Risk Factors

It commonly occurs during difficult labor and delivery or immediately postpartum (Table 25.6), exceptionally in a late postpartum or a nonlaboring woman [217]. In many cases, the amniotic fluid contains meconium [206]. Blunt abdominal trauma in advanced pregnancy is a risk factor. All cases (>50% of all traumatic) from MVAs with maternal blunt abdominal trauma were in a healthy woman during the third-trimester pregnancy [207, 218, 219].

### Pathophysiology

During labor, the amniotic fluid can enter the maternal circulation through small tears in the lower uterine segment, at the placental bed, or at the site of uterine trauma [217, 223]. There are two interlaced mechanisms. The mechanical one is that fetal mucin, lanugo hairs, and epithelial squames occlude the pulmonary microcirculation. The other mechanism includes biologically active substances in the amniotic fluid that initiate inflammatory, vasospastic, or procoagulative responses. These are arachidonic acid metabolites, endotoxin, and tissue factor [217]. Secondary effects are on cardiovascular and pulmonary function. The coagulopathy associated with AFE is likely mediated by factor VII activation (extrinsic pathway) induced by tissue factor [224].

Some claim that the entry of normal amniotic fluid into the maternal circulation has no hazards [208] or that a few fetal epithelial cells do not induce AFE symptoms entering maternal circulation [225].

### Clinical Presentation

The most common presentation of all-cause AFE is cardiac arrest. It typically presents with sudden hypoxia, hypotension with shock, altered mental status, and disseminated intravascular coagulation. Other common signs and symptoms are blood-tinged fluid/sputum in the mouth [214, 218], seizures, evidence of fetal distress, and maternal constitutional symptoms (fever, nausea, and headache). At the car crash scene, the condition is far worse than expected from the injuries sustained, with cardiorespiratory collapse.

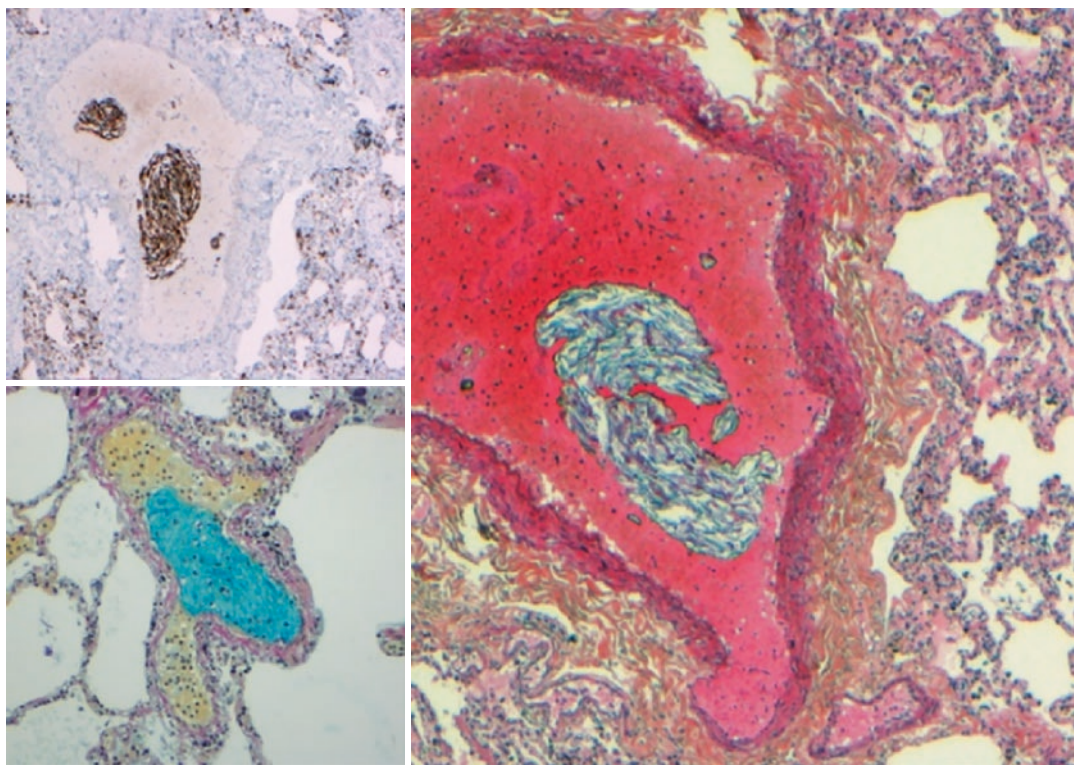
AFE should be suspected in every instance of the traumatized pregnant patient who develops signs of respiratory distress with or without right heart strain and disseminated intravascular coagulation.

### Diagnosis

No specific routine test confirms AFE. The diagnosis is clinical and essentially of exclusion. In pregnant trauma patients, other causes of collapse should be ruled out (air or thrombotic emboli, septic shock, hemorrhagic shock, anaphylaxis, UR, placental abruption, transfusion reaction, and toxicity of anesthetics). Laboratory tests may reveal hypoxemia and typical findings of DIC. Oil red O staining, Ayoub-Shklar staining, or the maternal vena cava blood sample can detect fetal fat, keratin, or formed elements of amniotic fluid. However, the application remains unsatisfactory due to its lack of sensitivity and the complexity of the procedure [222]. Bronchoalveolar lavage can reveal fetal squamous cells [213]. With maternal death, the diagnosis at autopsy shows congested lungs. The pulmonary vasculature contains mucus, epithelial squames, or lanugo hair (Fig. 25.22).

### Treatment

Maternal cardiac arrest mandates immediate CPR (see Sect. 2.3.3.1). Coagulation factors and blood transfusions may be needed to treat DIC and hemorrhage. Renal failure mandates temporary hemodialysis. Once spontaneous circulation



**Fig. 25.22** Lung histology shows epithelial squames inside an artery (HES stain, magnification 4×) (*Inset*). Immunohistochemical stain for Pan-cytokeratin high-

lights epithelial squames, and Alcian Blue-PAS stain highlights mucus. (Reproduced with permission from [214])

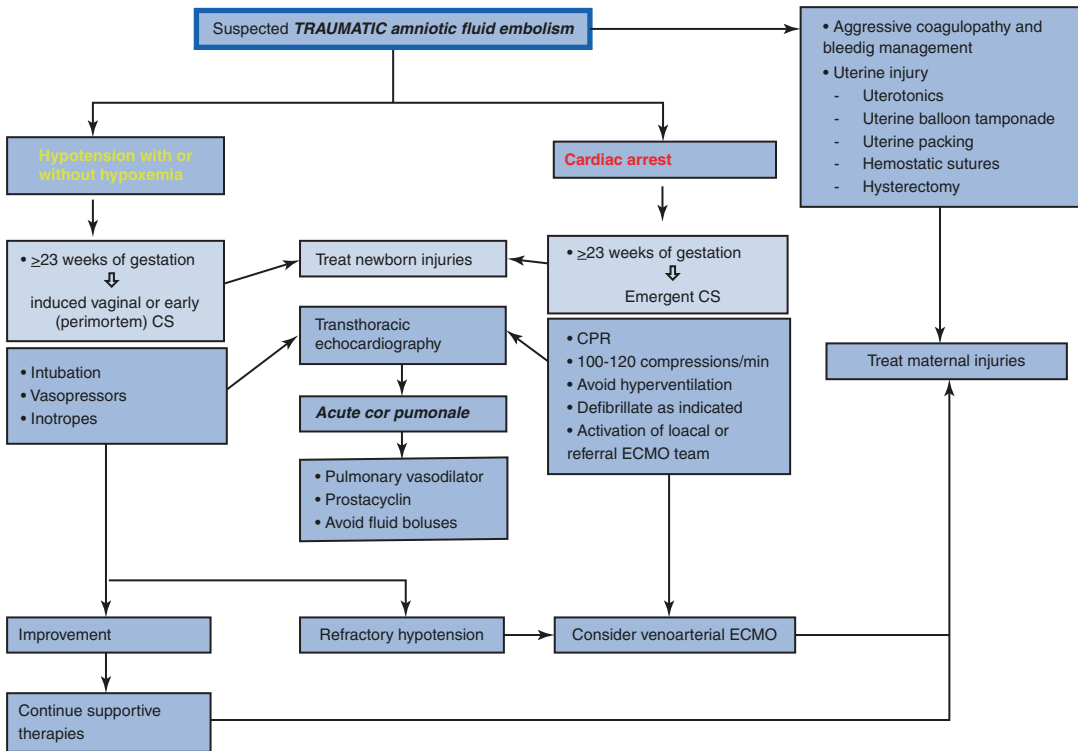
returns, many AFE survivors develop right ventricular failure (acute cor pulmonale) because of a sudden increase in pulmonary vascular resistance induced by systemic vasoconstrictors, such as endothelin-1 [224]. Immediate transthoracic echocardiography is recommended for early identification and management of acute right ventricular failure (Fig. 25.23). Medical management of right ventricular failure includes oral (through an orogastric tube if intubated) sildenafil, inhaled nitric oxide, and IV or inhaled prostacyclin (epoprostenol). Extracorporeal membrane oxygenation (ECMO) (see Sect. 2.1.4) can be used with CPR >10 min and a return of spontaneous circulation with severe right ventricular failure refractory to the medical management. Guidelines on diagnosis and treatment of AFE briefly mention ECMO but do not recom-

mend it based on the paucity of data and concerns for increased bleeding risks with anticoagulation [227]. ECMO may be started initially without the use of anticoagulation. After a few hours, once the bleeding risk is considered acceptable, anticoagulation, required for the ECMO circuit, may start gradually [224].

Emergency laparotomy is indicated in maternal trauma with hypotension and collapse. Sometimes, intra-abdominal injuries do not correlate with maternal clinical conditions [207, 219]. Emergency CS prevents further hypoxic damage to the fetus and facilitates maternal treatment.

### Prognosis

Initially, maternal mortality of all-cause AFE was 100%. Recently, it has lowered from 60% [228]



**Fig. 25.23** Treatment algorithm for traumatic amniotic fluid embolism during pregnancy. Early transthoracic echocardiography is usually performed after the return of spontaneous circulation. It may be used during CPR

through a subxiphoid view or during short pauses (<10 s) to check for a pulse. (Modified and reproduced with permission from [224, 226])

to 30% [221]. Extracorporeal membranous oxygenation lowered it further to 15% [226]. Maternal mortality from traumatic AFE is near 100%, usually during the first several hours [207, 211–215]. This is partly due to the unawareness of emergency physicians of this extremely rare and rapidly progressive obstetric condition. Also, when dealing with maternal abdominal trauma or polytrauma, physicians are concentrated on traumatic causes of hypotension, dyspnea, and collapse, resulting in a diagnostic and treatment delay with catastrophic consequences.

Extracorporeal membranous oxygenation lowered all-cause AFE fetal mortality to 15% [226]. Fetal mortality from traumatic AFE is also near 100% despite the performance of emergent CS [207, 211–215].

## 25.3.7 Diagnosis

### 25.3.7.1 Laboratory Findings

- **Base deficit (BD) >−6** has a probability of ≥95% for the absence of intra-abdominal bleeding,
- **BD ≤−6** and **increased pulse rate** indicate a markedly enhanced risk for intra-abdominal bleeding.

Decreased BD or increased pulse rate is highly sensitive for detecting internal bleeding [229, 230]. However, both studies focused on BD, and one [229] chose a BD of ≤−4 BD ≤−6 and had a

sensitivity of approximately 88.2% compared to ultrasonography (US), 76.5% [230]. The latter is because the US is not likely to detect most retroperitoneal or pelvic injuries [231]. However, the US has a positive predictive value of approximately 100% and a nearly equal negative predictive value with BD for detecting free fluid (see Sect. 25.3.7.3). Finally, BD correlates well with blood transfusion and laparotomy requirements (68.4% of patients with  $BD \leq -6$  indicated for blood transfusion compared with only 1.2% of patients with  $BD > -6$  and 57.9% of patients with  $BD \leq -6$  indicated for laparotomy compared with only 1.2% of patients with  $BD > -6$ ). All patients whose BDs were  $\leq -6$  had intra-abdominal bleeding and undergone a blood transfusion. A normal BD does not exclude intra-abdominal injury in blunt trauma patients, but a  $BD \leq -6$  should be considered a strong indication for abdominal evaluation. A BD of  $\leq -6$  has high sensitivity and specificity for detecting free fluid (FF) in patients with blunt abdominal trauma, as well as a high transfusion requirement and laparotomy in these patients.

Hemoglobin and hematocrit levels should be obtained in every patient with blunt abdominal trauma. In 5.4–8% of patients attended by trauma, an undiagnosed pregnancy is found [232]. Serum  $\beta$ HCG levels should be obtained for all females of reproductive age exposed to trauma [233] or selectively if the possibility of conception exists, if amenorrhea lasts  $>4$  weeks, or if the patient is unconscious. Protected X-rays should be obtained as possible.

Up to 16–43.5% of pregnant women with trauma were positive for a drug test (psychotropics, opiates, etc.) [38, 234]. Therefore, serum or urine samples of the most common drugs should be obtained from every pregnant trauma patient, especially with a head injury and changes in consciousness.

### 25.3.7.2 Plain Abdominal X-Ray

A plain abdominal X-ray confirms maternal skeletal trauma or maternal pneumoperitoneum from the rupture of the hollow viscus. The most common fractures include pelvic ring fractures and pubic symphysis diastasis (Fig. 25.24). Clinicians



**Fig. 25.24** In the 39th week of her first pregnancy, the patient fell from a standing position and landed on her buttocks with both hips in flexion, abduction, and external rotation. Pelvic X-ray shows the pubic symphysis diastasis. The sacroiliac joints could not be assessed. The fetal skull was high in the pelvis. (Reproduced with permission from [235])

should be cautious with diagnosing pubic symphysis diastasis in late pregnancy because it can result in the physiologic increase in elasticity of the pubic ligaments due to elevated levels of progesterone and relaxin [236].

### 25.3.7.3 Transabdominal Ultrasound

Focused abdominal sonography for trauma (FAST) is important for evaluating patients with blunt abdominal trauma. Sensitivities for detecting FF range from 42 to 100% [237, 238], while in pregnancy is 83% [239]. Some false-negative results are due to FAST performance early in the resuscitation process, when hemoperitoneum may not have accumulated to a detectable amount. A marked number of false-negative results (27.5%) are observed in patients with bowel and mesenteric injuries [237].

Some propose a CT for all hemodynamically stable patients with blunt abdominal trauma rather than FAST to prevent the underdiagnosis of intra-abdominal injury [238]. Only 7–8% of pregnant patients with trauma underwent a CT [237, 240]. The decision to perform a CT is arbi-



trary and may depend on equivocal objective findings that might result in an unnecessary laparotomy.

Although not as sensitive as CT, FAST has a distinct advantage over CT in the rapid triage of unstable patients with blunt trauma who cannot safely travel to the CT suite. Detection of FF or parenchymal abnormality results in a safer and faster disposition to the operating room than could be accomplished with CT or diagnostic peritoneal lavage. If no FF is detected, the patient may be transferred to the labor and delivery area for fetal monitoring and potential delivery. The US with contrast may be a viable alternative to CT.

### Maternal Pelvic Free Fluid

US examination of the pregnant abdomen to detect FF is more accurate than clinical examination. Varying amounts of FF have been detected during the menstrual cycle, with the greatest volume detected during ovulation [241, 242]. This FF is presumed to serve the teleological purpose of transporting the ovum by wave motion [241]. The prevalence of transient physiological FF on the transabdominal US in reproductive women ranges from 36 to 40%. The estimated mean volume ranges from 5 to 21 ml [241–245]. This phenomenon has been attributed to the following:

- Fluid secondary to follicular rupture [242],
- Ovarian fluid exudation secondary to increased capillary permeability under the influence of estrogen [242, 243],
- Blood secondary to retrograde menstruation [246].

The amount of peritoneal FF seemed to decrease significantly after the peak, near menstruation [242, 243]. The detection of FF in (a) both the abdomen and pelvis had the highest association with intra-abdominal injury, followed by (b) FF isolated to the abdomen, then (c) isolated to the pelvis, and the least (d) when there was no FF [247]. The FF most often occurs at the organ injury site and within the pelvis [248]. There is no difference in injury rate between those with isolated pelvic FF and those without

FF. Isolated pelvic FF is not likely to be associated with intra-abdominal injury [249]. These findings differ from Ormsby et al. in that isolated pelvic FF had a statistically significant higher injury rate than those without FF in pregnant and nonpregnant women. The discrepancy between previous findings [249] and findings by Ormsby et al. regarding isolated pelvic FF among nonpregnant patients may be due to several factors. Sirlin et al. had only 8% of pregnant patients. Ormsby et al. [247] had a larger sample size, with 16% pregnant women. Physiological FF is detected mainly during ovulation and a few days after ovulation in 36–40% of nonpregnant women [241]. Therefore, these women would not likely have US detectable amounts of physiological FF outside their ovulation period. Unfortunately, the authors did not query the menstrual history of their study subjects. Therefore, it is unknown if a greater percentage of women who were anovulatory or in a menstrual period when physiological FF is less likely to be detected.

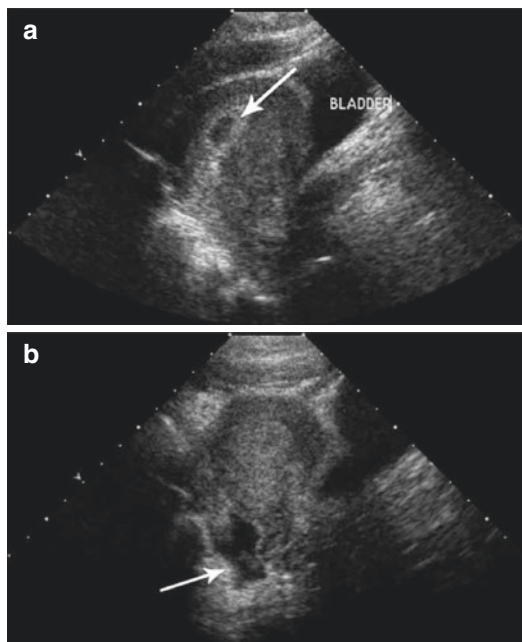
Transabdominal US is less sensitive than transvaginal US in detecting pelvic FF [244, 245]. The sensitivity of the pelvic view on the transabdominal US to detect FF is 73–129 ml [250], much larger than the average physiological amount of 7–21 ml [242–245]. Thus, any trace of FF in the pelvis on the FAST exam in the setting of blunt abdominal trauma may indicate pathological FF levels. Although more accurate for small volumes of pelvic FF, transvaginal US is impractical in the active trauma resuscitation setting. Furthermore, trauma patients undergoing FAST do not always benefit from having a full bladder. Therefore, FAST would not be expected to reliably detect small amounts of FF that would be detected during a detailed, comprehensive transvaginal US. In pregnant patients, small amounts of pelvic FF may be missed due to a mass effect of the enlarging uterus [251]. The US was less sensitive to detecting intra-abdominal injury in pregnant vs. nonpregnant female patients [237]. Another possible explanation of missed pelvic FF is inadequate bladder distention during the US, which provides an adequate acoustic window [252]. Patients with blunt abdominal trauma often have a Foley catheter,



which decompresses the bladder. Of the nine false-negative cases in pregnancy, 67% were due to placental abruption, and the US is not sensitive in detecting placental abruption [253]. Careful clinical correlations such as gestational age, significant vaginal bleeding, fetal distress, or severe abdominal pain should be made for these patients. If placental abruption was excluded, pregnant patients without FF would have an injury rate of 1% with no change for the group where the fluid was isolated to the pelvis. Isolated pelvic FF is the second most common true-positive fluid accumulation pattern [237].

The ability to distinguish between physiological and traumatic FF has been previously addressed. Siirlin et al. reported isolated FF in the cul-de-sac in 56 patients, and only two had injuries, but they made no distinction between pregnant and nonpregnant patients [249]. They concluded that isolated FF in the pelvis was likely physiological. In another study, 54% of the false-positive US examinations in pregnant and nonpregnant patients revealed isolated FF in the pelvis [237]. Also, the study revealed three patients with undiagnosed ectopic pregnancies that ruptured after their traumatic events. Ectopic pregnancy has steadily increased over the past three decades [254], and serum  $\beta$ HCG should always be obtained in women of reproductive age. The transvaginal US is the imaging method for detecting an ectopic pregnancy, but less is known regarding transabdominal US [255]. FF in the left upper quadrant, in both upper quadrants, or diffusely is associated with splenic injuries [237, 248].

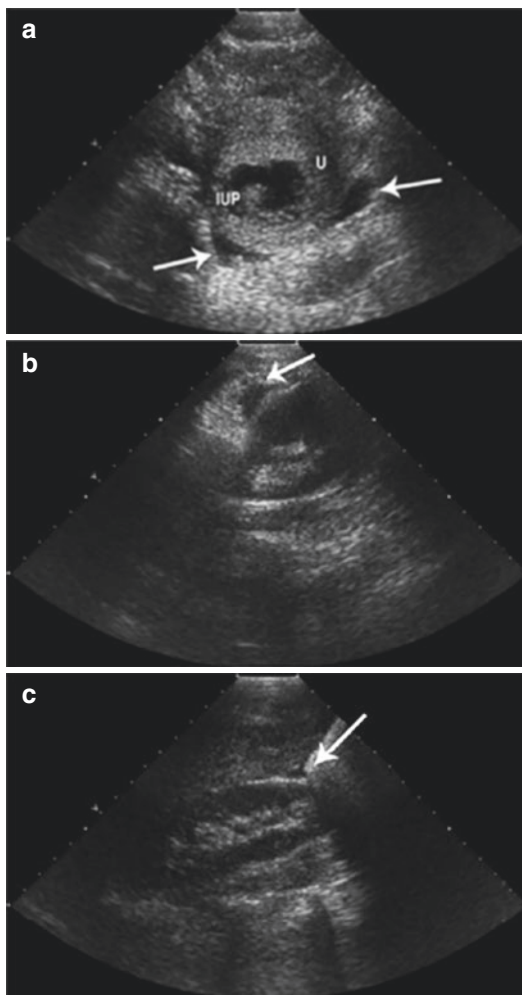
The flow dynamics show that FF tends to flow from the left to the right upper quadrant rather than down the left paracolic gutter into the pelvis. One explanation may be that bleeding from the spleen first accumulates in the left and then progresses to the right upper quadrant because the phrenocolic ligament acts as a relative barrier to the movement of FF to the left gutter [256]. It also appears that FF from the right upper quadrant flows down the right paracolic gutter rather than toward the left upper quadrant, perhaps



**Fig. 25.25** A pregnant female in the first trimester involved in a motor vehicle crash with physiological free fluid (FF). (a) A longitudinal ultrasound scan of the pelvis shows early intrauterine pregnancy (arrow). (b) A longitudinal pelvic ultrasound scan demonstrates FF (arrow) in the cul-de-sac. (Reproduced with permission from [247])

because of the gravity dependence of the right paracolic gutter and pelvis. The most common locations of FF accumulation in pregnant patients of all gestational ages are in the left and right upper quadrants and the pelvis (Figs. 25.25 and 25.26).

However, the US depicted pelvic FF in pregnant patients in the third trimester, and the sensitivity of FAST was the highest in the first trimester of pregnancy. One explanation may be that the compression of intra-abdominal structures, specifically the paracolic gutters, by the expanding uterus makes detecting FF more difficult in the paracolic gutters and pelvis [257]. The fetus is well protected against injury from blunt trauma because it is encased in a fluid-filled structure [13]. Intra-abdominal injuries in pregnant patients are common to the spleen or placenta, necessitating precipitous delivery or resulting in fetal demise [237]. Thus, the shear forces present



**Fig. 25.26** A first-trimester high-speed motor vehicle accident with spleen laceration. (a) A transverse scan of the pelvis with an empty bladder shows early intrauterine pregnancy and bilateral free fluid (FF) (arrows) adjacent to the uterus. (b) A transverse scan of the left upper quadrant demonstrates FF (arrow). (c) A longitudinal scan of the right upper quadrant demonstrates FF (arrow) in the hepatorenal fossa. IUP intrauterine pregnancy, U uterus. (Reproduced with permission from [247])

in even low-force injuries such as falls cannot be discounted. It is recommended that the US, and fetal monitoring (>20 weeks' gestation), should be used routinely in pregnant patients with trauma. Continuous fetal monitoring is more sensitive but less specific than the US for detecting placental abruption [65].

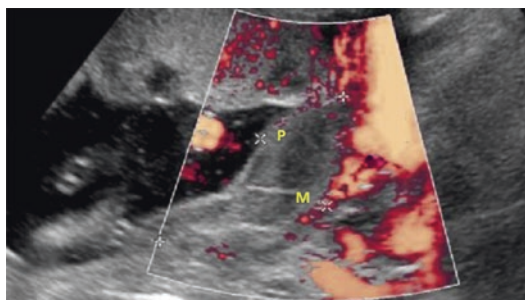


**Fig. 25.27** Placental abruption. An emergency ultrasound performed in the trauma bay reveals the presence of anechoic pockets representing hematoma separating the placenta (P) from the myometrium (M). (Reproduced with permission from [258])

FAST examination to detect FF in pregnant trauma patients has specificity and accuracy of >90% but a relatively low sensitivity (61%), demonstrating that the FAST examination remains an appropriate screening tool for intraperitoneal hemorrhage but that it does not rule out intra-abdominal pathology [237].

### Placental Abruption

The sensitivity of the US to identify post-traumatic abruption is only 40–50% [22, 65]. Therefore, the absence of visualization of subchorionic hemorrhage or a retroplacental clot (Figs. 25.27 and 25.28) on the US in the presence of clinical symptoms like abdominal pain mandates further continuous fetal monitoring. A low threshold to intervene if signs of fetal distress appear or abdominal CT should be performed. Acute placental abruptions can be seen on the US as an echogenic retroplacental mass, which becomes hypoechoic in 1–2 weeks, mimicking uterine fibroids.



**Fig. 25.28** Placental abruption. A 21-week pregnant patient. A heterogeneous collection is interposed between the placental edge (*P*) and the myometrium (*M*). The collection lifts the placental edge away from the underlying myometrium. (Reproduced with permission from [258])

#### 25.3.7.4 Cardiotocography

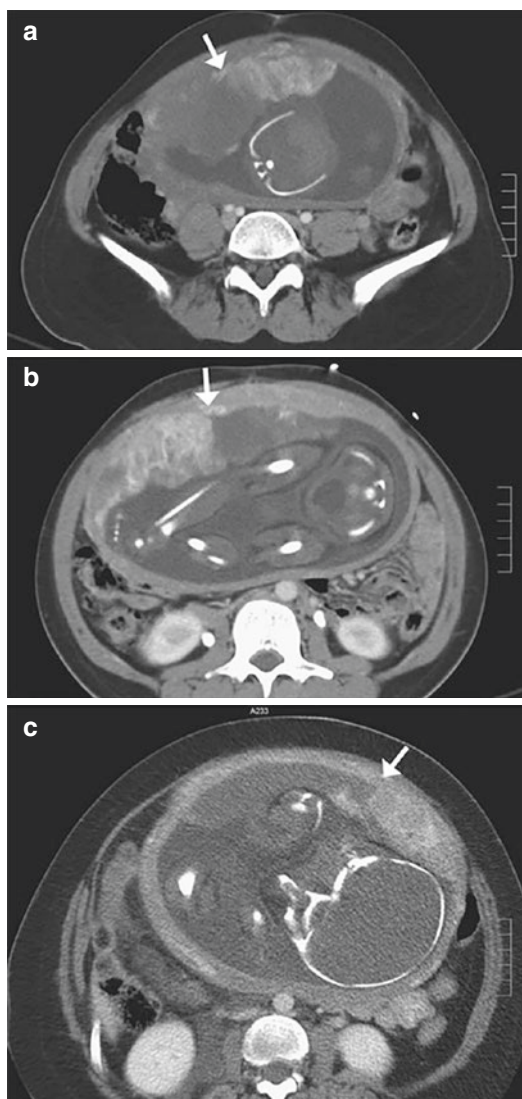
Ultimately, complete placental separation and fetal demise will occur as the placental abruption continues. Depending on the size of the initial clot, placental abruption might not be infrequently asymptomatic in its early stages. Due to the high thromboplastin concentration in the surrounding trophoblastic tissue, local DIC is likely to expand the clot. With the expansion of the retroplacental clot, uterine activity will usually emerge. With >8 contractions/h and the absence of reassuring fetal monitoring, there is a 25% chance of placental abruption after blunt abdominal trauma [65]. Changes in fetal CTG, such as bradycardia (<110 bpm), loss of beat-to-beat variation, or sinusoidal patterns, may indicate placental injury, fetal hypoxia, or fetal blood loss.

#### 25.3.7.5 Abdominal CT

##### Placental Abruption

There have been few CT studies of normal and abnormal placental anatomy [259, 260], which may lead to an unsatisfactory evaluation of placental abnormalities. Because the normal gravid uterus and physiological changes during pregnancy often confound the interpretation of CT studies, it is helpful to define the anatomical variations associated with normal placental development [261].

True placental abruptions were characterized by large, contiguous, and retroplacental or full-thickness areas of low enhancement that form



**Fig. 25.29** CT shows traumatic placental abruptions. (a) Right-sided placental hematoma at 23 weeks of gestation. (b) At 29 weeks of gestation, absence of perfusion in the anterior placenta. (c) At 36 weeks of gestation, heterogeneous placental enhancement and relative area of decreased enhancement anteriorly correlate with abruption. White arrows, the border between nonperfused and perfused regions of the placenta. (Reproduced with permission from [262] under the CC Attribution License)

acute angles with myometrium (Fig. 25.29). Some abruptions remain undetected likely due to the lack of systematic evaluation of the placenta or when the retroplacental hematoma is isodense to the normally enhanced placenta [263]. False-positive results required additional

obstetrical monitoring overnight. This is an acceptable cost compared to the catastrophic consequences of missing an abruption. Aberrations in fetal heart rate correlate with the severity of placental abruption [264]. They may be a valuable tool to differentiate between false-positive results and true abruptions diagnosed by CT. The sensitivity of the CT for placental abruption is near 100%, with somewhat lower specificity [262].

## 25.3.8 Treatment

### 25.3.8.1 Conservative Treatment

The optimal duration of maternal hospital monitoring of minor or no apparent injuries following an MVA is 24 h, without any adverse impact on complication rates [6]. After a visit, careful evaluation following repeated abdominal trauma and costly routine hospitalization for 24 h or more appears to be dispensable as in single-event cases [22]. Patients without premature uterine contractions or abdominal tenderness and normal findings in the clinical evaluation, in the screening US, and the continuous 4 h nonstress test may safely be sent home and instructions for a proper follow-up in the outpatient clinic.

The management of pregnant trauma patients is related to four injury groups [43]. The first is comprised of injured women who are unaware that they are pregnant (incidental pregnancy). Since routine radiographic studies have the greatest teratogenic potential in early pregnancy, a pregnancy test should be obtained from all trauma patients of reproductive age. The second group is pregnant women of less than 24–25 weeks of gestation, where the primary focus is solely on the mother since the fetus has not yet reached the border of viability. The third group comprises pregnant women at a gestational age beyond the border of viability. For this group, monitoring, support, and clinical consideration include the mother and fetus. The fourth group is comprised of severely injured women in a perimortem state. Early CS may facilitate maternal resuscitation and increase the fetal survival rate. A radiologic examination is contraindi-

cated because perimortem CS should be performed within 4–5 min of maternal (unsuccessful) CPR.

### 25.3.8.2 Interventional Radiology

Bleeding into the pelvis (zone 3 of the retroperitoneum) is challenging to control surgically. The current recommendations in the hemodynamically unstable, nonpregnant patient with severe pelvic trauma and no other identifiable source of bleeding include angiographic embolization of pelvic or retroperitoneal bleeding, mainly via hypogastric arteries [265], or pelvic packing.

Operative fixation, apart from bone stabilization, also stabilizes retroperitoneal hematoma. Percutaneous embolization is indicated in a postpartum patient without an indication for the operative fixation of the pelvic fracture (see section “[Pelvic Fracture Treatment](#)”) or continuing bleeding after operative fixation (Fig. 25.30).

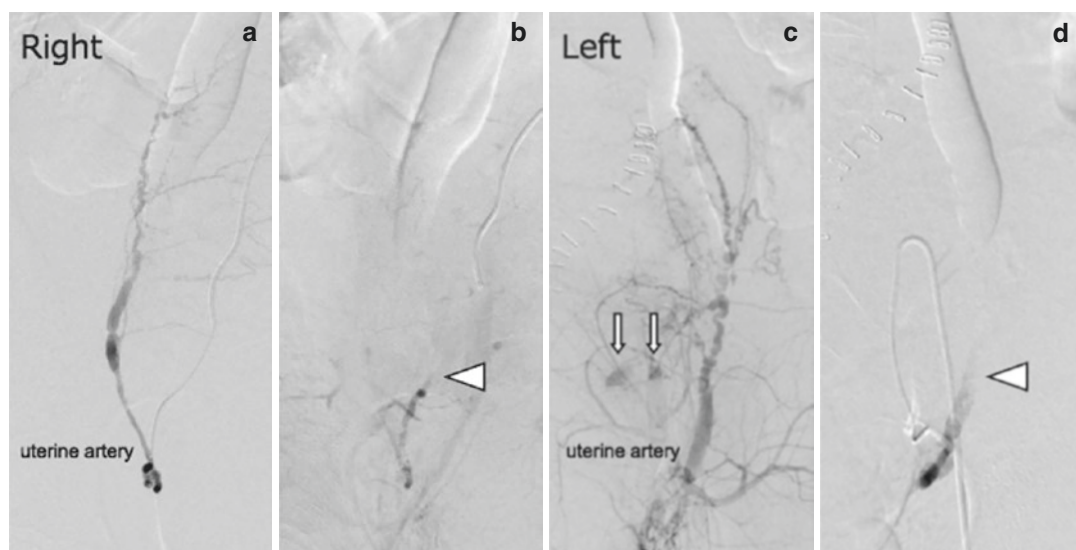
### 25.3.8.3 Surgical Treatment

#### Initial Stabilization

The management of maternal cardiac arrest is presented in Sect. 2.3.3.1. Rapid maternal respiratory support is critical; anoxia occurs more quickly (especially in advanced pregnancy): (1) as oxygen consumption increases by almost 20% during pregnancy to meet the increased metabolic demands of the placenta, fetus, and maternal organs [267], and (2) as functional residual capacity may be significantly reduced due to elevation of the diaphragm. This leads to increased minute ventilation leading to compensatory respiratory alkalosis and decreases the maternal capacity to buffer acidosis from shock. This leads to more rapid respiratory decompensation, particularly with chest trauma. Supplemental oxygen maintains maternal oxygen saturation >95% to ensure adequate fetal oxygenation (Fig. 25.31) [271, 272].

The evaluation of the fetus begins after the mother has been stabilized. Supplemental oxygen and IV fluids are administered initially and are continued until hypovolemia, hypoxia, and fetal distress resolve [108]. Two large-bore (14–16 gauge) IV lines should be placed in a severely





**Fig. 25.30** Arteriography before and after uterine artery embolization. (a) The right uterine artery was completely recanalized. (b) The right uterine artery was completely embolized using a gelatin sponge (arrowhead). (c) The

left uterine artery was completely recanalized and showed extravasation (arrow). (d) The left uterine artery was completely embolized using a gelatin sponge (arrowhead). (Reproduced with permission from [266])

injured pregnant woman [271]. These measures maximize uterine perfusion and oxygenation for the fetus [108]. In animal studies, the fetal arterial  $pO_2$  or fetal heart rate improvements slower with saline or lactated Ringer's solution than with blood replacement attesting to restoring oxygen-carrying capacity and blood volume [45, 47].

Because of the increased blood volume late in pregnancy, the mother may not show typical signs of hypovolemia, even with the loss of a large blood volume (up to 2000 ml). However, uterine perfusion may still be compromised.

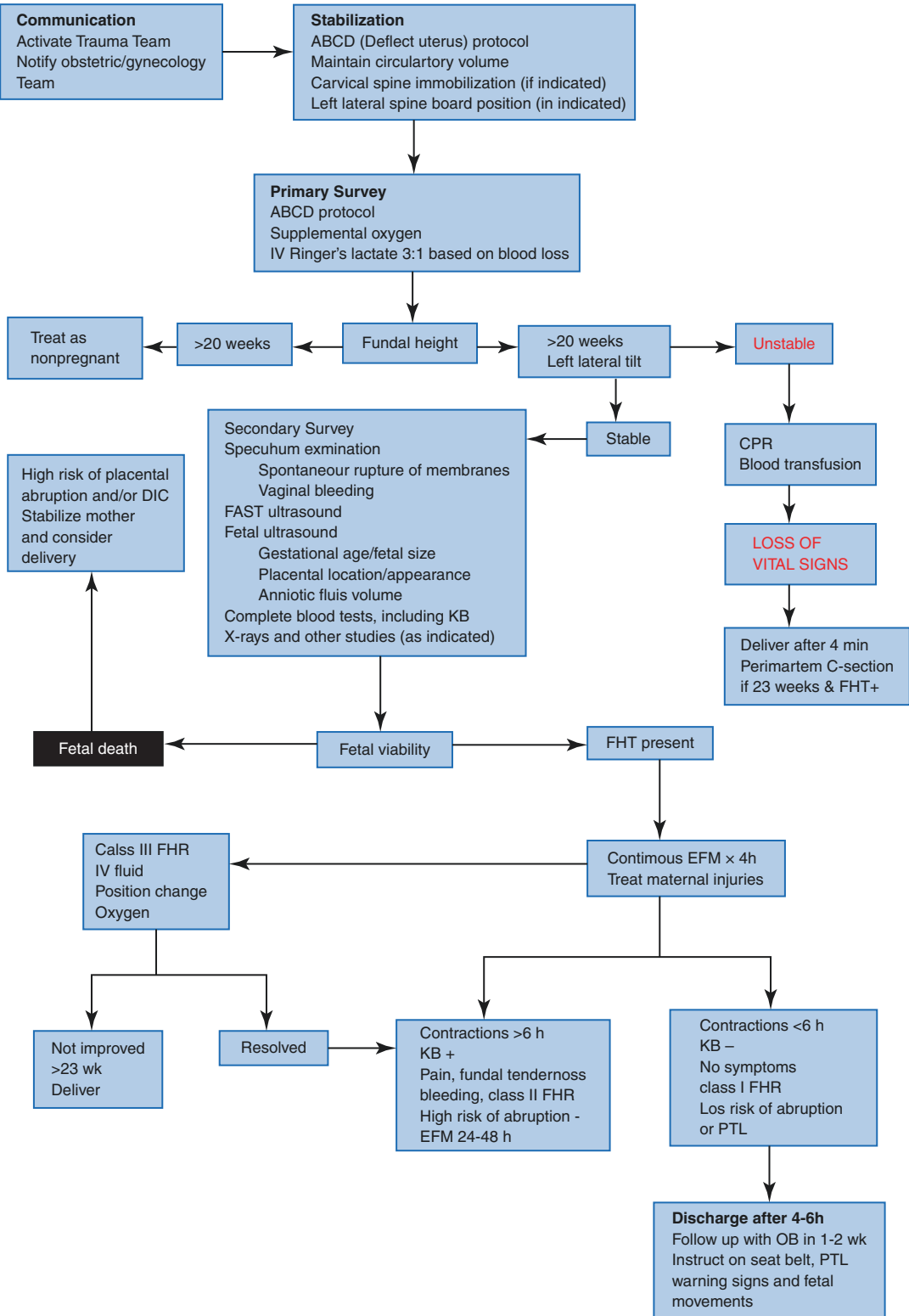
Uterine blood flow may decrease by up to 30% before the mother demonstrates clinical signs of shock. Therefore, blood transfusion should be initiated when significant or suspected blood loss has occurred. Crystalloid effectively improves neonatal oxygenation if there is evidence of maternal hypotension. However, if hypotension is suspected to be due to bleeding, O-negative blood is the resuscitation fluid of choice.

Significant blood loss can occur in the uterine wall or retroperitoneal space without external bleeding. After 20 weeks of gestation, the uterus may compress the great vessels when a pregnant woman is supine. This compression can cause a decrease of up to 30 mmHg in maternal systolic blood pressure, a 30% decrease in stroke volume [272], and a consequent decrease in uterine blood flow [108]. Manual deflection of the uterus laterally or patient placement in the lateral decubitus position avoids uterine compression [108]. Vasopressors in pregnant women should be used only for intractable hypotension unresponsive to fluid resuscitation because of their adverse effect on uteroplacental perfusion [271].

### Secondary Assessment

After initial stabilization, other maternal injuries are evaluated. Doppler or US assesses fetal heart tones (FHTs). If FHTs are absent, resuscitation of the fetus should not be attempted. There were no fetal survivors in a series of 441 pregnant trauma patients with initially absent FHTs [273]. When FHTs are present, gestational age is determined by fundal height, history, Leopold's maneuvers, or US [273]. The US most accurately determines gestational age. Determination of





**Fig. 25.31** Algorithm for the management of the pregnant woman after blunt (abdominal) trauma. (Modified from [268–270]; KB Kleihauer-Betke test, FHT fetal heart

tones, EFM electronic fetal monitoring, PTL preterm labor). If the Kleihauer-Betke test is positive, the treatment should follow the instructions in Fig. 25.21

fetal viability is subject to institutional variation: an estimated gestational age of 24–26 weeks and an estimated fetal weight of 500 g are commonly used thresholds of viability. Only viable fetuses are monitored [273] because no obstetric intervention will alter the outcome with a previable fetus. The physical examination findings in the pregnant woman with blunt trauma are unreliable in predicting adverse obstetric outcomes [15, 65]. Pregnancy induces physiological changes in women (Table 10.4). For example, maternal blood pressure does not accurately reflect uterine perfusion or fetal injury [54, 232, 274] because pregnant women can lose up to 30% (2000 ml) of their blood volume before vital signs change. Blood transfusions should be administered according to standard guidelines, but the mother's Rh status must be considered. If it is unknown, Rh– blood should be administered. Invasive hemodynamic monitoring should be considered early during resuscitation to ensure adequate volume resuscitation [108]. Compared with nonpregnant persons who experience trauma, pregnant women have a higher incidence of severe abdominal injury but a lower incidence of the chest and head injuries [5]. Maternal pelvic fractures, particularly in late pregnancy, are associated with bladder injury, urethral injury, retroperitoneal bleeding, and fetal skull fracture [108]. After 12 weeks of gestation, the maternal uterus and bladder are no longer exclusively pelvic organs and are more susceptible to direct injury [107]. Skull fracture is the most common direct fetal injury, with a mortality rate of 42% [54]. Altered mental status or a severe head injury after trauma in a pregnant woman is associated with increased adverse fetal outcomes [45]. Placental abruptions usually occur from 16 weeks of gestation onward [107]. Some signs of placental abruption, including spontaneous rupture of membranes, vaginal bleeding, and uterine tenderness, are infrequent after trauma [5, 22, 65, 66]. Although associated with maternal and fetal morbidity [40, 172], these signs are 52% sensitive and 48% specific for adverse fetal outcomes [15].

### Pelvic Fracture Treatment

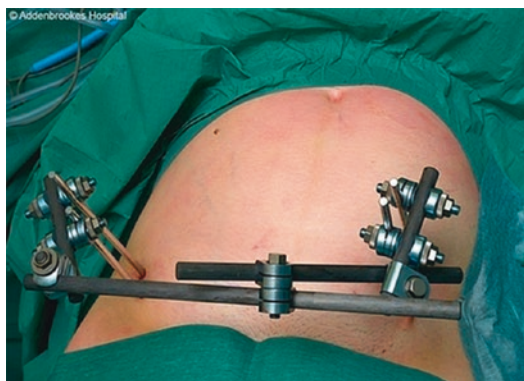
There are several unique aspects to the closed reduction of the pregnant patient's pelvis. The

gravid uterus acts as a compressive device on the inferior vena cava (IVC) when the pregnant patient is supine, inhibiting venous return and decreasing cardiac output. Close reducing an open book pelvic fracture with a sheet or a binder may worsen this problem by increasing the compression of the gravid uterus on the IVC, further decreasing venous return. If the patient is too unstable to be placed into the full left lateral decubitus or a concurrent spinal injury prevents safe left lateral decubitus positioning, a roll or wedge may be placed under the right side of the backboard in spinal immobilized patients, or the bed rotated with the right side up [29]. Management of pubic symphysis disruption is generally nonoperative. It includes circular compression of the pelvis with a symphysis belt brace/binder (Fig. 25.32). This is accompanied by bed rest in a lateral decubitus position for additional diastasis compression. Progressive moderate physiotherapy follows, including pelvic floor strengthening exercises. Ambulation is assisted with crutches in a four-point gait or using a walker.

Pelvic and acetabular fracture surgery is infrequent in pregnancy [71, 276–279]. Considerations against surgery during pregnancy are due to (1) increased complication rate [276] and (2) potential intraoperative uterine injury. In some cases, the mother's general condition, affected by other injuries, coagulopathy, or hemodynamic instability, does not permit surgical intervention



**Fig. 25.32** Postpartum placement of symphysis/pelvic belt brace compressing pelvic symphysis diastasis. (Reproduced with permission from [275])



**Fig. 25.33** Supra-acetabular external fixator applied for open book/isolated anteroposterior type 2 (APC2) injury under the Young-Burgess classification. (Reproduced with permission from [280])

[71]. Acetabular fracture treatment was reported in 83.3%, with skeletal traction and open reduction with internal fixation performed equally frequently [276]. Unstable pelvic ring fractures can be safely treated with open and percutaneous osteosynthetic techniques (Fig. 25.33), resulting in favorable pregnancy outcomes [71, 277–279]. Vertically unstable posterior pelvic ring fracture using a low-exposure technique and imaging restricted to the posterior ring can be performed [278]. External fixation is recommended with (1) unstable lesions, (2) inadequate reduction, (3) diastasis of  $>4$  cm [281], or (4) vertical displacement of the pubic rami associated with a widening of the sacroiliac joint means a disruption of the pelvic ring [282]. For severe, intractable pain, an open reduction and internal fixation may be necessary [283].

External fixation of unstable pelvic fractures in pregnant patients is a viable option with good maternal and fetal outcomes. Pins must be placed to provide a stable construct, allow uterine (and abdominal) enlargement, and safe access for subsequent CS [280].

Postpartum management of pelvic symphysis diastasis is presented in Fig. 25.34. There are no recommendations for antepartum traumatic pubic

symphysis diastasis. If operative treatment is indicated in the absence of fetal distress or placental abruption and delivery within 3 weeks, vaginal delivery is recommended, followed by operative reduction of the diastasis. If delayed fracture surgery is to be contemplated, it should probably be performed within 3 weeks of injury, as the quality of reduction diminishes after 3 weeks as in the general population. If CS is indicated, a standard Pfannenstiel incision is adequate for both CS and operative reduction.

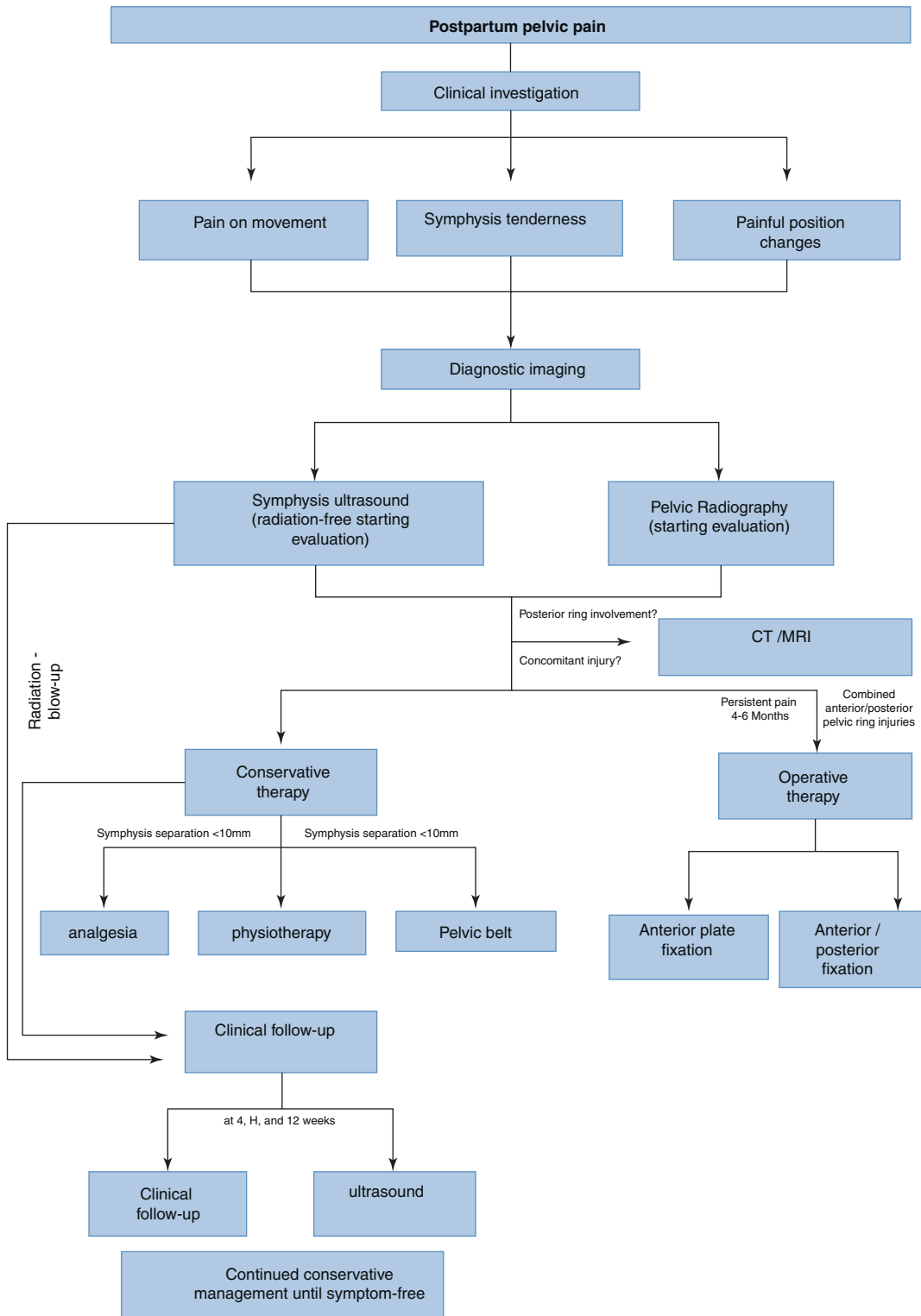
### Damage Control Surgery

*The only weapon with which the unconscious patient can immediately retaliate upon the incompetent surgeon is hemorrhage.*

(William Stewart Halsted, 1912)

*Damage control surgery* is the rapid termination of operation after controlling life-threatening bleeding and intestinal spillage, followed by the correction of physiological abnormalities which precede definitive management of initial injuries [284]. It creates a stable anatomic environment to prevent the patient from progressing to an unsalvageable metabolic state. Patients are more likely to die from metabolic failure than failure to complete organ repair [285]. This strategy involves a staged approach to multiply injured patients. Damage control surgery avoids or corrects the lethal triad of hypothermia, acidosis, and coagulopathy during or before definite injury management. Harlan Stone first described the concept of abbreviated laparotomy in 1983 [286]. Any laparotomy was terminated with temporizing measures when coagulopathy was noted.

These involved abdominal cavity packing to stop the bleeding and scheduled return to the operating room. The term “damage control” (Rotondo and Schwab, 1993) outlines a three-phase approach for patients with major abdominal injuries [287]. Phase one controls hemorrhage and contamination with rapid intra-abdominal packing and stapling of intestinal ends, followed by temporary abdominal closure. Phase two, in the ICU, addresses restoring a physiological environment—temperature, coagulation, and oxygen delivery. Phase three occurs within 24–36 h, with the removal of abdominal packs, restoration of intestinal continuity, and definitive



**Fig. 25.34** Algorithm for postpartum pubic symphysis separation. (Reproduced with permission from [275])

surgery with abdominal closure. The concept of damage control was expanded (Johnson, 2001) with the fourth phase at the beginning called “ground zero” [288]. The principles of “ground zero” damage control include rapid transport to the hospital and early decision-making to facilitate hemorrhage control, prevent hypothermia, and utilize massive transfusion protocols. Accepted clinical and laboratory parameters for the application of principles of damage control surgery are the following:

- Hypotension: SBP <90 mmHg,
- Hypothermia:  $T < 34^{\circ}\text{C}$ ,
- Coagulopathy: activated partial prothrombin time (aPPT) >60 s,
- Acidosis: pH <7.2 or arterial base deficit (BE)  $\geq 8$ ,
- Major intra-abdominal vascular injury,
- The associated need for management of extra-abdominal life-threatening injury (e.g., concomitant thoracic injuries).

Reports on damage control surgery in pregnancy are rare and mostly limited to liver injuries, spontaneous liver rupture complicated by HELLP syndrome (see Chap. 26), and splenic injuries [289]. Pregnancy should not influence the decision to employ principles of damage control in a severely injured woman. Hypotension, coagulopathy, and acidosis develop in a pregnant woman later, necessitating a more proactive approach.

One of the main controversies of damage control surgery in pregnant women concerns the delivery timing. Since fetal delivery in maternal extremes should be part of resuscitation to recruit the uteroplacental blood volume to the maternal circulation, delivery of a term or near-term fetus should be regarded as part of the damage control approach. The situation with severely preterm infants is more complex. Assuming that damage control surgery is exclusive in catastrophic abdominal or thoracic injuries with ongoing bleeding, the hemodynamic instability of the mother mandates all possible resuscitative efforts, including CS of a premature fetus. However, pre-

term delivery is not mandatory in damage control surgery [290]. A fetal gestation could be safely prolonged after 28 weeks of gestation.

#### 25.3.8.4 Obstetric Management

##### Fetal Assessment and Monitoring

The obstetric US should be performed to assess fetal viability, fetal age, fetal well-being [16], and potential fetal injuries (see Chap. 5). Evaluation of fetal trunk and extremity movement, fetal breathing activity, amniotic fluid volume, and fetal heart rate changes with fetal movement will establish fetal well-being. Approximately 24% of pregnant trauma patients admitted to the hospital will deliver at the trauma hospitalization [11, 291]. Therefore, a viable fetus of  $\geq 24$  gestational weeks requires cardiotocographic (CTG) monitoring after maternal trauma, even without signs of maternal abdominal injury [22, 67].

Continuous electronic fetal monitoring is more sensitive in detecting placental abruption than the US, intermittent monitoring, KB test, or physical examination [67].

Monitoring is initiated immediately after maternal stabilization [67, 108, 273] because most placental abruptions occur shortly after trauma [5]. The ideal duration for electronic fetal monitoring is unclear [15, 30, 54, 67]. The recommendation is a minimum of 4 h of CTG [65], while others recommend 6 h [67, 291]. This should be extended to 24 h if, at any time during the first 6 h, there is more than one uterine contraction every 15 min ( $\geq 5/\text{h}$ ), uterine tenderness, nonreassuring fetal CTG, vaginal bleeding, rupture of the membranes, or any severe maternal injury (Fig. 25.31). This widely used protocol has a sensitivity of 100% ( $>20$  weeks of gestation) for predicting adverse outcomes within 4 h [65].

Occasional uterine contractions are the most common finding after trauma in pregnancy [5, 15, 65, 66]. These occasional contractions are not associated with adverse fetal outcomes [5, 67] and resolve within a few hours in 90% of cases



[65]. However,  $\geq 8$  uterine contractions per hour for more than 4 h are associated with placental abruption [65]. With placental abruptions after trauma, the fetal mortality rate is 67–75% [5, 40]. If significant placental abruption occurs, a viable fetus should be delivered immediately, and 69% of fetal deaths can be prevented by CS [292]. Bradycardia or repetitive late decelerations unresponsive to intrauterine resuscitation require immediate delivery in a stable mother [273].

Approximately 70% of patients required more than 4 h of fetal monitoring because of continued contractions ( $\geq 4$ h), abnormal laboratory values, or vaginal bleeding. All patients discharged at the end of 4 or 24 h had similar outcomes to noninjured control patients [65]. Fetal tachycardia or a nonreactive nonstress test prolongs monitoring to 24 h. Some recommend prolonged electronic fetal monitoring with high-risk injury mechanisms: automobile vs. pedestrian and high-speed MVAs [67]. No evidence supports routine electronic fetal monitoring for more than 24 h after noncatastrophic trauma [15]. It can prevent only a few perinatal deaths and is most helpful in determining the reassuring fetal status and appropriate discharge [15]. Abnormal tracings (3.1% of pregnant women with traumatic injury) are not reliable in predicting adverse fetal outcomes (sensitivity 62%, specificity 49%) [5, 15]. In contrast, normal tracing has a negative predictive value of 100% when combined with a normal physical examination [15].

Patients who enter preterm labor and those at risk of developing contractions (i.e., gestational age  $>35$  weeks, victims of assault, and pedestrians hit by motor vehicles) should also be monitored for 24 h [67]. If formal continuous fetal monitoring is not available, periodic Doppler measurement or bedside US of a fetal heart rate is an appropriate temporary substitute. The fetal US may reveal liver [293] or brain injury [131, 294].

Beware of the potentially tachycardic maternal heart rate in pregnant trauma victims. Comparing the fetal heart rate heard with the Doppler with the maternal pulse on the cardiac monitor can help ensure that it is the fetus's pulse being measured.

## Maternal Pelvic Fractures

The recommended method of delivery for pelvic fractures during pregnancy depends on the presence of initial fetal and maternal distress, the degree of fetal maturity, the maternal ISS, the displacement of the pelvic or acetabular fracture, and the eventual course of labor. Because these fractures tend to heal within 8–12 weeks, vaginal delivery should not be contraindicated after fractures in the first and second trimesters. Pubic ramus fractures adjacent to the urethra or bladder, severe lateral compression, and acute pelvis fractures with marked displacement may be relative indications for CS if labor starts in a viable pregnancy. Eastman, in 1958, stated that CS would be necessary for 5–10% because of pelvic deformity after a fracture. Others stated that vaginal delivery through a recently fractured pelvis is not attended by severe complications and should be permitted without gross pelvic deformity [295, 296]. Bladder and urethral injuries have been reported after delivery through a recently fractured pelvis [296]. The separation or displacement of fractures around the symphysis pubis jeopardizes the urethra and bladder when the presenting part descends during labor [297]. Fortunately, vaginal delivery was successful in 75% of pelvic fractures in the third trimester [276]. All patients with acetabular fractures had a delivery at term [298]. MRI or CT estimation of displacement of pelvic fractures could determine the delivery method and potential of simultaneous obstetric and orthopedic operation.

## Postpartum Care

### Placental Abruption

After delivery, a patient's hemodynamic status should be carefully monitored. Based on central hemodynamic monitoring indices, hemoglobin concentration, and urine output, judicious use of transfusion or diuretics may be required. If vaginal delivery is accomplished quickly without trauma, prompt restoration of the hemostatic mechanism usually results. Even in the most severe cases, clinically evident coagulopathy usually resolves by 12 h after delivery. Fresh-frozen plasma or platelet transfusions occasionally are necessary to hasten the process.

Suboptimal clotting may occur at delivery, and wounds must be inspected for hematoma formation. Early ambulation reduces the phenomenon of rebound hypercoagulability in patients recovering from DIC [299]. Pulmonary status must be monitored, especially with rapid induction of general anesthesia and risk for aspiration pneumonia. Reversible acute renal failure can result from hypovolemia and vasospasm.

### Emergency Cesarean Section

Emergency CS is indicated if [271]:

- Maternal resuscitation fails/cardiac arrest,
- Uterus interferes with the examination and repair of maternal injuries,
- A viable fetus suspected of having direct injury,
- Maternal shock,
- Possible exsanguinations from any cause,
- Irreparable uterine injury,
- Fetal distress in a viable fetus,
- Unstable thoracolumbar spine injury,
- Amniotic fluid embolism,
- Viable pregnancies (>24 weeks).

Decreased placental enhancement to <25% on one slice of a CT image is the marker of a placental abruption very likely to require emergency CS [300, 301].

Fetal indications for emergency CS are described in Chap. 5.

### Perimortem Cesarean Section

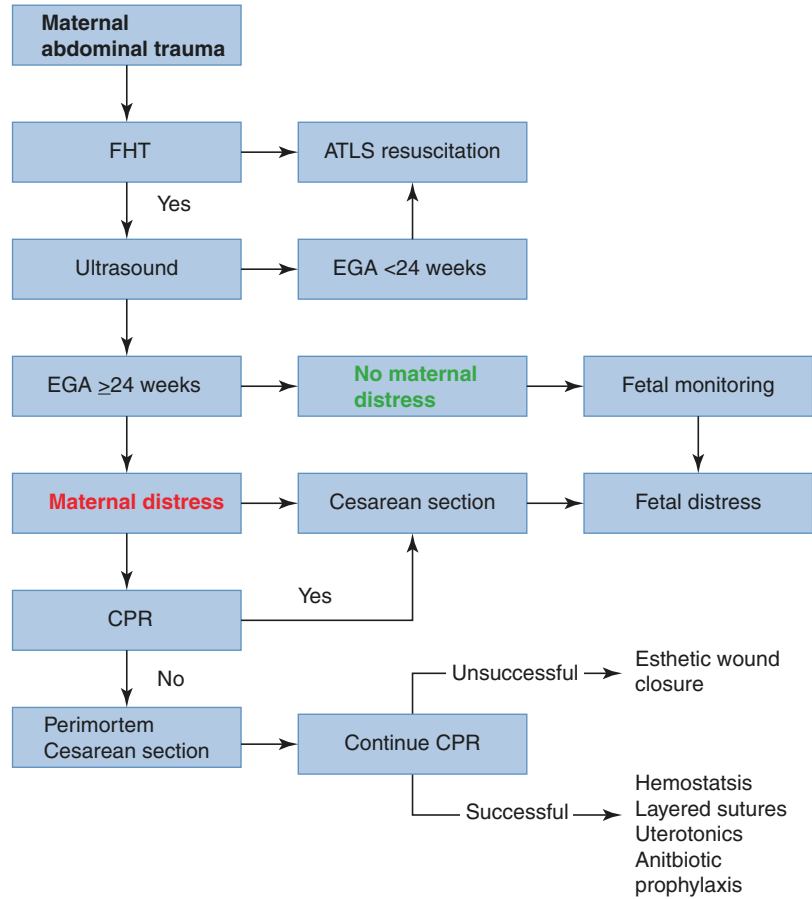
Historically, the operation was performed in Egypt as early as 3000 BC [302]. Sage Sutra, who practiced around 600 BC and is one of the founders of ancient Hindu medicine, referred to postmortem abdominal delivery in his medical treatise *Sutra Samhita* [303]. It is possible that in both Egypt and India, this procedure was ordained by law [302]. In Greek mythology, Apollo, the god of medicine, killed his wife Coronis, King Phlegyas' daughter, a mortal woman. He killed her in anger because she slept with a stranger

while pregnant. Apollo took pity on his unborn son and ripped Asclepius from Coronis' womb when her body was already in the burning pyre. A poet Pindar described this episode [304]. Postmortem CS was spread with the Roman decree (*Lex Cesare*, or the law of Caesar—decreed by Numa Pompilius). The purpose of this ancient law was based on religious rituals to keep the fetus from being buried with the mother rather than attempts for newborn survival. In 237 BC, the first reported infant who survived a postmortem CS was Scipio Africanus, who subsequently became the Roman general who defeated Hannibal [305]. The first mention of postmortem CS in anticipation of fetal rescue was by Bernard de Gordon (1260-1318), a Montpellier physician, in 1305, published in 1491 [306]. Then, in 1483, a woodcut reproduction showed a baby being removed from its dying mother's uterus by CS (Fig. 25.35). It was not until 1500 AD that Jacob



**Fig. 25.35** A baby being removed from its dying mother's womb via Cesarean section. Reproduction of woodcut, 1483. (Reproduced with permission from [308] from under CC Attribution License)

**Fig. 25.36** Clinical algorithm for the emergency cesarean section and perimortem cesarean section. The pregnant trauma patient is assessed for fetal heart tone (FHT) and estimated gestational age (EGA). With FHT and EGA  $\geq 24$  weeks, fetal monitoring is required. Fetal or maternal distress mandates the emergency cesarean section. Perimortem cesarean section is performed during maternal cardiopulmonary resuscitation (CPR). ATLS advanced trauma life support. (Modified and reproduced with permission from [273, 310])



Nufer sectioned his wife with the survival of the mother and the infant [305]. In his book in 1545, Charles Estienne (1504–1564) provided another example of a postmortem (cause unknown) CS to deliver a living neonate [307].

Katz et al. in 1986 defined the first modern approach to perimortem CS [309]. Perimortem CS is emotional and often futile and should only be considered when (Fig. 25.36) [108, 309]:

- Uterine size exceeds the umbilicus or gestation  $>24$  weeks,
- Evidence of fetal heart activity (Doppler or M-mode US),
- Unsuccessful maternal CPR  $<4$ – $5$  min (up to 15 min if fetal vital signs persist).

Restoration of maternal and fetal circulation is the goal of adequate resuscitation (see Sect. 2.3.3.1). Perimortem maternal revival after delivery is due to the relief of vena cava compression and more effective CPR after pressure below the diaphragm is relieved. Optimization of cardiac output and perfusion of the uterus via left thoracotomy, open cardiac massage, and perimortem CS should be considered. With emergency department thoracotomy, the aorta is often cross-clamped, adding to the uterine hypoperfusion and decreasing the likelihood of a favorable fetal outcome [29].

The trauma or abdominal surgeon and obstetrician decide on perimortem CS; hemostasis and antisepsis become secondary issues. Perimortem CS should not be delayed in obtaining consent despite being an invasive emergent procedure. Routine preparations (such as the placement of a

urinary drainage catheter or surgical preparation of the abdomen) are time-consuming and irrelevant. The most skilled in CS should perform perimortem CS. Neonatologists must be available. The procedure covers emergency delivery during the ongoing maternal CPR, where the mother has no sign of recovery afterwards with or without infant survival [311].

Prepare skin with an antiseptic solution and a sterile drape if immediately available. Insert a Foley catheter to empty the bladder. These two steps can be skipped if only 5 min are left for CS. The wound can be cleansed, and antibiotics administered if the mother survives. Obstetricians and neonatologists should be consulted. The appropriate incision for a perimortem CS is midline from the xiphoid or slightly below it to the symphysis pubis (Fig. 25.37) with a scalpel. Incise through subcutaneous tissue until the linea alba. Lift linea alba with toothed forceps. Incise through all layers of the abdominal wall and peritoneum (Fig. 25.37). Retract the abdominal wall and the bladder with retractors. When the uterus is identified, a vertical uterine incision with a scalpel is made (Fig. 25.37). The uterine incision is extended first in the superior and then in the inferior direction with a blunt tip scissor. The fetus is additionally protected with the remaining fingers (Fig. 25.37). If the placenta is anterior, it should be incised. Use a clamp to rupture the amniotic membranes and then deliver the infant's head. Suction the mouth and nose with a bulb syringe (Fig. 25.37). Deliver the shoulders, followed by the torso and extremities. Secure the umbilical cord with a hemostat or umbilical cord clamp 10 cm distal to the fetus and a second clamp 2 cm distal to this clamp. With scissors, incise the umbilical cord between the two clamps, cut the cord, and begin infant resuscitation. If the patient is still alive or regains vital signs, deliver the placenta (Fig. 25.37). Begin with an oxytocin infusion at 20 U in 1 L at 10 ml/h. Bladder repair is also performed if the mother survives. The uterus should be closed in two layers following delivery with a 2-0 or 1-0 suture. Skin staples or a running stitch is an acceptable method of skin closure for a dead mother.

Maternal resuscitation should continue simultaneously with CS, with some chances for survival [313]. Immediately after spontaneous delivery, cardiac output rises by 60–80% of prelabor values [314], and after CS by 30% of prelabor values [315]. The smaller increase associated with CS is due to anesthetic-induced hypotension and blood loss, usually averaging 1000 ml. Before 23 weeks' gestational age, the delivery may not improve maternal venous return. Therefore, aggressive maternal resuscitation is the only indicated intervention [270]. When maternal salvage is possible, prophylactic antibiotics and meticulous hemostasis must be achieved during layered closure of the abdomen.

Maternal CPR must be continued until perimortem CS is accomplished.

Fetal prognosis after perimortem CS is described in Sect. 25.4.4.

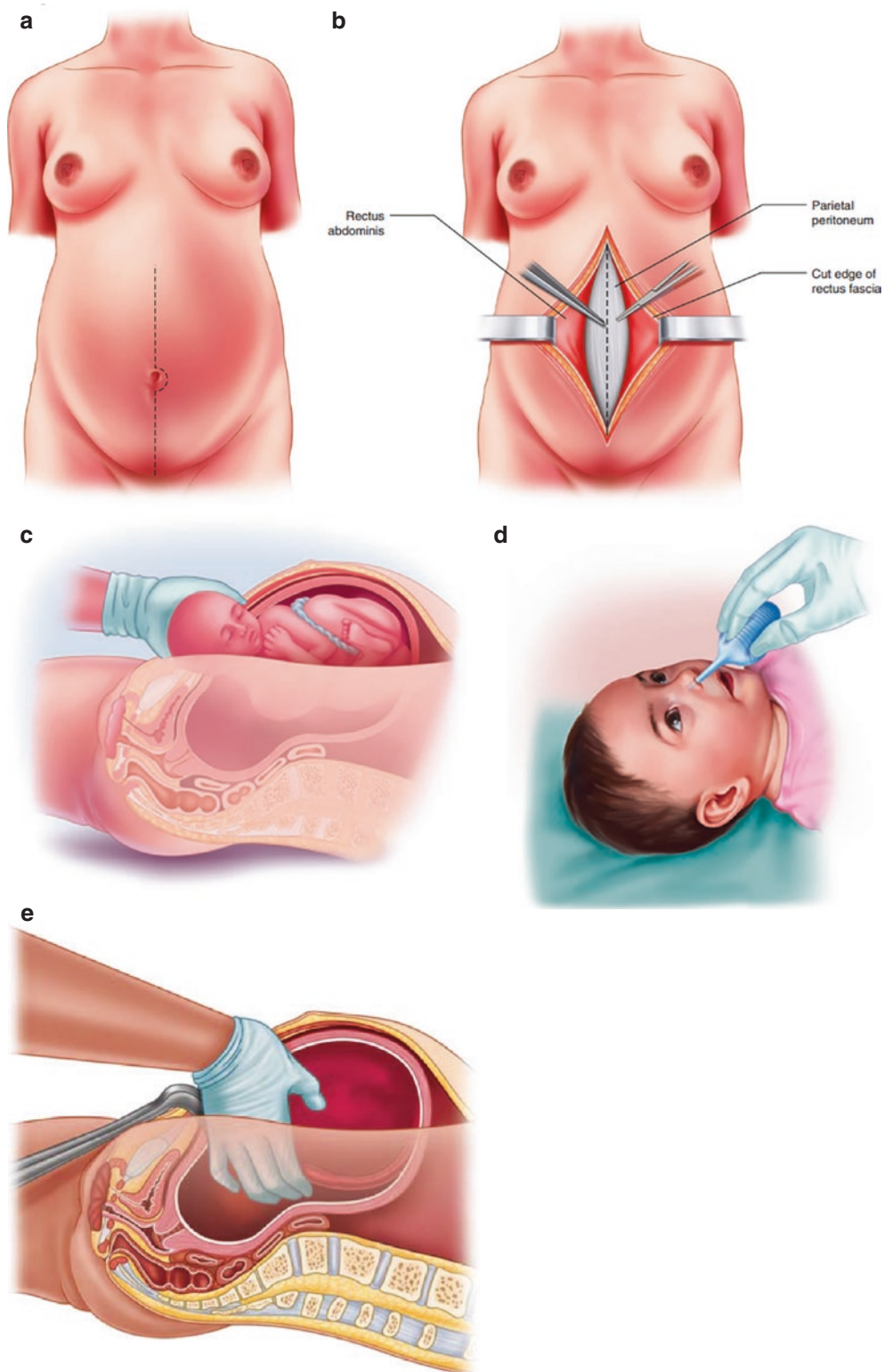
### Salvageable Infant

A salvageable infant is defined by an estimated gestational age of  $\geq 26$  weeks and the presence of FHTs. The survival rate is 75%. Survival is independent of maternal distress but related to fetal monitoring and early recognition of fetal distress. Without FHTs, fetal mortality is 100%. This supports the premise that fetal viability is related to the presence or absence of FHTs on admission.

The urgent CS is not considered as FHT could not be heard during the initial evaluation of the mothers who died.

The presence of FHTs is a simple, rapid, reproducible, and profoundly important marker of fetal viability. The recommendation is that the Doppler assessment of FHTs is a component of the primary survey performed on trauma patients during the third trimester of pregnancy. This should be accomplished simultaneously with





**Fig. 25.37** (a–e) Step-by-step procedure of perimortem Cesarean section (see text for details). (Reproduced with permission from [312])



assessing maternal circulatory integrity during the ABCs of trauma resuscitation. If FHTs are absent, the pregnancy should be ignored, and treatment should be directed solely at maternal survival. The survival of 23–25 weeks' gestation infants increases with each additional week [316]. However, the overall neonatal survival rate for infants born during this early gestational period remains less than 40% [273]. Of those who survived, 6–40% have moderate to severe disabilities, and many have neurobehavioral dysfunction and poor spontaneous school performance [317].

As noted previously, high-admission FHR values may be expected for patients arriving at the ED soon after the start of maternal hemorrhage. Furthermore, obstetric practice in the nontraumatic setting has documented baseline FHR to be less predictive of fetal stress than baseline variability and periodic change assessment of the FHR [318]. Lack of knowledge of baseline FHR before trauma and the wide variability (20 bpm) of FHR under normal physiological conditions [319] further degrade the predictive utility of admission FHRs. Although it is ideal for informing the prospective parents regarding the fetal outcome and the financial and emotional consequences of profound prematurity, this is not possible in the trauma setting where the patients are often critically ill or sedated, families are unavailable, and the decision-making process is obscure. Consequently, it is recommended that fetal viability in the trauma patient should be defined at 26 gestational weeks [273]. Even in the most profoundly injured mother, manifested by an ISS >25, fetal survival could be 78% [273]. This same critically ill population had a maternal survival rate of only 44%, illustrating the need for emergency CS at the first indication of fetal distress (FHR <100 bpm, prolonged deceleration >60 s, or recurrent late decelerations). Although maternal survival in the presence of an ISS <16 was 100%, fetal survival was only 73% [273], supporting previous evidence that even minor maternal injury can result in fetal death [320]. ISS does not significantly differ between pregnant occupants with subsequent spontaneous abortions and uneventful pregnancies. However,

the scores were significantly higher among pregnant occupants whose fetuses died, including stillbirth and newborn death within 1 month of delivery [95].

ACOG has published guidelines on performing CS for mothers in extremis following medical disasters, i.e., AFE, cardiac arrest, etc. These could be extrapolated to similar physiological insults to a pregnant trauma patient. Fetal survival rates of 70% have been reported for fetuses of at least 25 weeks of gestation delivered within 5 min of maternal death [309]. Even higher fetal survival was documented, with nearly 100% maternal survival. The causes of fetal death were complications from prematurity and anoxia [321]. There are no specific data for abdominal trauma, perimortem CS, and fetal or maternal survival.

### 25.3.9 Prognosis

In the past, most causes of maternal death were obstetric due to a lack of prenatal care and inadequate assistance during delivery. A significant reduction in maternal mortality was noted because of improved medical services, hospital deliveries, and reduced parity. Although a remarkable decline in maternal mortality in the USA during the twentieth century was evident, little progress has been made during the last two decades in the twentieth century [322]. In fact, according to the Centers for Disease Control and Prevention, the maternal mortality rate has slightly increased over the past few years, reaching 13/100,000 births in 2004. Trauma complicates up to 7% of all pregnancies and is the leading cause of nonobstetric maternal deaths, accounting for around 46% of all maternal deaths [13, 323–325]. Pregnancy and childbirth remain serious, life-threatening events for many women in low-income countries, with maternal deaths contributing to as many as 25% of all deaths of women of reproductive age [326]. The death of a woman in childbirth signifies far more than the tragic loss of a single life; it can threaten the survival of the whole family, especially the newborn baby and other young children. The risk for preg-

nancy in “minor” or noncatastrophic trauma is still significant—preterm labor 8%, placental abruption 1%, and fetal death 1%. Maternal mortality is about 9% for those with major trauma [5], while the fetal death rate is  $\geq 20\%$ .

### 25.3.9.1 Blunt Trauma

Trauma is the most common cause of maternal mortality, with an incidence of 46.3% [13]. In other words, 24% of patients sustaining a major blunt trauma in pregnancy died [327]. The major injury includes a shock at admission, skull fracture, cerebral contusion or intracerebral hemorrhage, spinal column fracture or injury, chest injury necessitating thoracotomy or tube thoracostomy, and injury of the abdominal viscera or genitourinary tract treated operatively or a pelvic fracture. In 1971, maternal mortality of 7% was reported in severe automobile injuries and a 14% injury rate in surviving mothers [124].

Head injury is the most common cause of maternal death, followed closely by hemorrhagic shock [4, 12, 163, 328].

Maternal hemorrhagic shock carries a maternal mortality rate of 66.6% [329]. Serious injuries (high ISS) result in a higher mortality rate (Fig. 25.38), but this mortality rate in pregnant women is comparable with nonpregnant. When

injury type is examined, maternal and fetal death is highest, with internal injuries to the thorax, abdomen, and pelvis.

### Fetal Outcome

Pregnant women after minor trauma have a favorable pregnancy outcome. Pregnancy outcomes in terms of the incidence of placental abruption, gestational age at delivery, mode of delivery, postpartum complications, and neonatal outcomes do not differ between women who experience minor trauma compared to pregnant women who do not [200, 330]. The chance of delivering preterm is probably higher among women injured in the second trimester than those injured close to the term [11, 330].

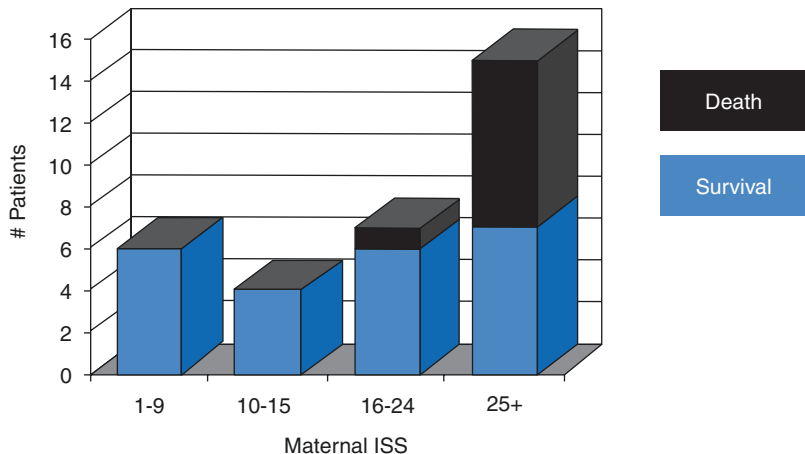
Repeated minor blunt abdominal trauma is rare but could induce preterm uterine contractions and labor. Delayed severe complications such as placental abruption are infrequent after noncatastrophic abdominal trauma due to a fall [22, 291] and did not appear to be a more prominent issue after a second such event with a lag of 1 week or more [331].

### 25.3.9.2 Motor Vehicle Accidents

#### Maternal Outcome

More than 90% of injuries to pregnant women from MVA are minor [20, 44]. Compared with nonpregnant women, pregnant women admitted after an MVA suffered less severe injuries and

**Fig. 25.38** Maternal mortality in 1966 by injury severity score shows that maternal injury-adjusted mortality is compatible with established norms. ISS injury severity score. (Reproduced with permission from [273])



consequently required fewer therapeutic interventions and a shorter hospital stay. The reasons are [20]:

- More likely to seek medical attention,
- More likely to be admitted for observation and monitoring of the fetus,
- MVA of a less severe nature,
- More cautious and refrain from potentially life-threatening behaviors,
- More likely to be wearing seat belts.

The widespread use of maternal observation is supported by the fact that of all pregnant trauma patients in an emergency department, only 8% would have been admitted in the absence of pregnancy [66].

Pregnant women with a collision-related MVA were at increased risk of requiring genitourinary surgery (OR 1.45). When restricted to women with a fracture, pregnant women were even more likely to require genitourinary surgery (OR 2.93), as well as require a blood transfusion (OR 1.21) [20].

The in-hospital mortality rate for pregnant women was less than for their nonpregnant counterparts [20]. Estimates for maternal deaths from MVAs 30 years ago range from 5 to 34% [13, 25, 86, 126, 324, 325]. The common cause was uncontrollable bleeding [86]. Recent studies show even 0% maternal mortality [161]. This is due to speed limit restrictions, improved car deformation zones, car pre-safe systems, increased use of seat belts, and an increasing number of car airbags. During the MVA admission, most women who had no adverse outcomes were admitted for 1 day and were discharged home undelivered. However, for those requiring delivery ( $\geq 20$  weeks of gestation) during admission, the pregnancy complication rate was significantly higher than for women who did not have an MVA. Over a quarter had a placental abruption, and over half delivered  $< 37$  weeks of gestation [6]. The primary cause of death was uncontrollable hemorrhage. Severely injured women have a 17-fold increased risk for placental abruption [162].

**Table 25.7** Types of injuries by women hospitalized for a motor vehicle accident in Washington State, 1989–2001

| Injury classification                   | Nonsevere injury (%) | Severe injury (%) |
|-----------------------------------------|----------------------|-------------------|
| Fractures, dislocations, sprains        | 53.4                 | 81.0              |
| Intracranial injuries                   | 9.7                  | 25.0              |
| Internal injury of the chest            | 0                    | 26.2              |
| Internal injury to the abdomen          | 2.9                  | 20.2              |
| Internal injury of the pelvis           | 1.0                  | 2.4               |
| Open wound                              | 17.5                 | 41.7              |
| Blood vessel injury                     | 0.3                  | 3.6               |
| Superficial, contusion, crushing injury | 53.4                 | 26.2              |
| Nerve and spinal cord injuries          | 0.3                  | 1.2               |

(Reproduced with permission from [32])

Unbelted pregnant women (1989–2001) had a two times higher complication rate than belted pregnant women at the time of MVA (Table 25.7).

Maternal pelvic fractures carry maternal mortality of 7–29% [71, 72, 276]. Mortality rates are not affected by the fracture classification (simple vs. complex), the fracture type (acetabular vs. pelvic), the trimester of pregnancy, or the decade studied [276]. Automobile-pedestrian collisions had a statistically higher maternal mortality rate than pregnant women involved in vehicular collisions, which had a statistically significant trend toward a higher fetal mortality rate. Most maternal deaths occurred from associated injuries, particularly acute bleeding [276]. Increasing maternal injury severity and associated injuries significantly increase maternal mortality.

### Fetal Outcome

Maternal injuries are the highest predictor of fetal injuries and fetal mortality. Severely injured women have a 20-fold increased risk of fetal death [162]. The primary causes of fetal death are maternal death and placental abruption [12, 332]. Pregnant women who did not wear a seat belt during an MVA have 1.3 times increased risk for a low birth weight infant and 2.8 times increased risk for fetal death [78]. The type of maternal seat

**Table 25.8** Obstetrics and Gynecology, Washington State (2002–2005): maternal and perinatal outcomes associated with airbag deployment among pregnant women in a motor vehicle accident

|                           | Airbag (%) | No airbag (%) |
|---------------------------|------------|---------------|
| <i>Obstetric outcome</i>  |            |               |
| Preterm labor             | 15.7       | 10.3          |
| Placental abruption       | 2.0        | 1.6           |
| Labor induction           | 31.9       | 21.6          |
| Cesarean delivery         | 26.8       | 24.1          |
| <i>Perinatal outcome</i>  |            |               |
| Gestational age <37 week  | 11.1       | 10.0          |
| Birth weight <2500 g      | 8.7        | 8.2           |
| Small for gestational age | 11.6       | 9.8           |
| Meconium at delivery      | 6.5        | 5.7           |
| Fetal distress            | 5.6        | 6.0           |
| Respiratory distress      | 2.5        | 1.6           |
| Fetal death               | 1.0        | 0.3           |

(Modified and reproduced with permission from [333])

belt during MVA is the predictor of fetal death. With a shoulder harness, the fetal death rate was 8% compared to 50% when a lap belt was used. The improvement in fetal survival with a shoulder harness was due to the greater surface area over which the decelerative force was dissipated and the prevention of maternal forward flexion.

The airbag activation during MVAs caused a higher percentage of preterm childbirth and fetal mortality (Table 25.8). This indicates that the airbag negatively affects pregnant women during MVAs. However, because of the large differences in the number of pregnant women (three times more when an airbag was not activated than it was) included in the research, the possibility of certain deviation is present, which reduces differences in the impact of an airbag to pregnant women. It is possible to conclude that airbag has no negative impact on pregnant women during MVAs.

### 25.3.9.3 Repeated Blunt Abdominal Trauma

The rate of emergency room visits for blunt abdominal trauma was 5.4/1000 deliveries encompassing 270 pregnant women with one or more noncatastrophic abdominal trauma during the second and third trimesters due to MVAs, falls, and assaults. Only one study analyzed repeated blunt abdominal trauma. Only 1.9% of women sustained more than one blunt but direct

blow to the abdomen due to falls during the second and third trimesters [331]. The time between the events ranged from 1 to 4 weeks. The median hospitalization time per admission was 2 days, while all five patients stayed in the hospital for 27 days during pregnancy. Extension to more than 24 h surveillance was exclusively due to preterm uterine contractions after the incident. Preterm contractions were noted in 60% (3/5), and one delivered at 34 weeks. Repeated blunt abdominal trauma rarely occurs in gestation. It does not warrant clinical management except for symptoms and signs of premature rupture of membranes, vaginal bleeding, placental abruption, or intra-uterine growth changes. Restriction or antepartum death was encountered. The time between the last trauma and the delivery ranged from 2 to 10 weeks. All patients delivered spontaneously. One patient, an epileptic woman, suffered from an increase in partial seizures with disturbances in motor function. Lack of compliance with the prescribed antiepileptic drug regimen could not be ruled out as contributing to the rationale for the four extended hospital stays of that patient following the seizures. The KB test was positive in that patient only after multiple traumatic events and negative in the rest of the patients, including a patient who delivered preterm after two trauma events 1 week apart.

## 25.4 Penetrating Trauma

### 25.4.1 Incidence and Pathophysiology

Of all abdominal traumas in pregnancy, penetrating trauma is present in 9–16% [334]. Of those, 73% were handgun-, 23% knife-, and 4% shotgun-related [334]. Maternal visceral injury with penetrating injuries is 19–38% [335]. Penetrating trauma in pregnancy has a different injury pattern than blunt trauma. The size of the uterus in pregnancy makes it the most likely organ to be injured, followed by the fetus and placenta. The gravid uterus may act to protect the abdominal viscera—only 18% of women with gunshots sustain a visceral injury [336]. The uterine muscle acts as a buffer to absorb missile

energy and prevent injury to the viscera beyond the uterus [337]. Although the gravid uterus protects other viscera, stabbings into the upper abdomen can cause serious injury, especially to compressed bowel loops or the overlying diaphragm. The latter is particularly dangerous in pregnancy, if unrecognized, because of the possibility of subsequent bowel strangulation, which has much higher mortality rates in pregnancy (25–60%) than in the nonpregnant patient (16–20%) [169].

#### 25.4.1.1 Gunshot Wounds to Uterus

The first report of a gunshot wound to the uterus is from the 1600s by Ambrose Pare, and the first recorded case of a gunshot wound to the pregnant uterus appeared in 1845 [338] and then by Verrier in 1888. A review 10 years later collected 45 reports since 1845 [339]. Until 1968, 16 additional cases were described [42]. Experience at the American University of Beirut Medical Center, throughout 16 years of civil war (1975–1991), revealed another 14 cases [340], now with a total of approximately 100 cases [341, 342].

There are two pathophysiologic mechanisms for gunshot wounds. First is the direct damage by the projectile itself, and the destruction depends on the caliber and type of the projectile and the distance between the projective and the victim. The second is the blast effect created by passing a high-velocity projectile in a closed fluid-filled compartment. The high pressure caused by the mass movement of displaced fluid could result in the UR. The shock wave ahead of the projectile has a concussive effect depending on the ratio of air and fluid-filled spaces. The obvious injury is caused by compression and shearing force [343]. On the contrary, there is a protective role of the uterus. The uterus diminishes the velocity of a missile and thereby decreases its ability to penetrate other organs and the fetus. The musculature of the pregnant uterus is thickened and dense, and most of the traumatic force is transmitted to the muscle. Moreover, the amniotic fluid and the fetus also slow the bullet, diminishing injury to other maternal organs.

Because of the anatomical alterations caused by the enlarging uterus, the pregnant woman responds differently to abdominal trauma than

the nonpregnant woman. The gravid uterus works as a maternal shield, protecting more vital maternal structures from injury. As a result, the incidence of visceral injuries in pregnant women with penetrating abdominal trauma is 16–38% [335], significantly lower than that in the general population, where it is 80–90% with anterior abdominal gunshot wounds and may exceed 95% with evidence of peritoneal penetration [344].

#### 25.4.1.2 Stab Wounds to the Uterus

Reported instances of uterine stab wounds during pregnancy are even rarer. Guadagnini reported the first case of a stab wound of the gravid uterus in 1930 [345]. A literature review disclosed 35 cases until 2019. The typical patient stabbed in pregnancy is 18–28 years of age, almost constantly during the second half of pregnancy. In nearly 100%, the tool was a knife [346–348]. Approximately 50% of fetuses were injured [346–348].

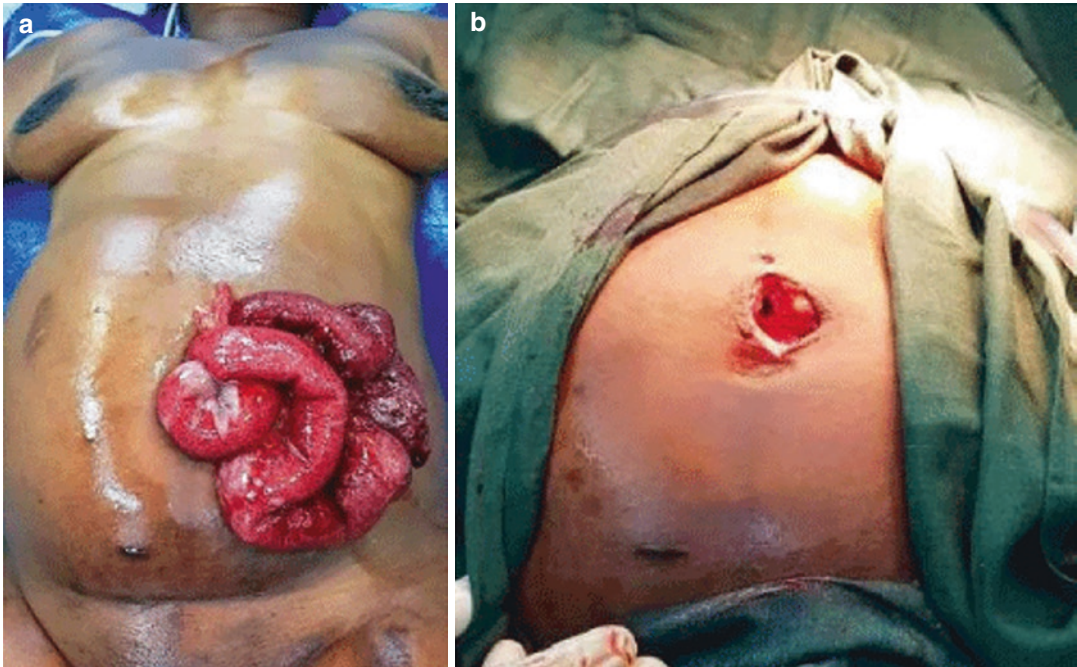
### 25.4.2 Clinical Presentation

Clinical presentation depends on the type of injury, the number of wounds, and the degree of organ injuries. With gunshot wounds, an entry and exit wound(s) should be noted (Fig. 25.39). These can predict the bullet path and possible intra-abdominal injuries. High-velocity projectiles are often unpredictable, and multiple wounds can exist concomitantly. Uterine injury results in continued or intermittent vaginal bleeding [349].



**Fig. 25.39** Maternal entry gunshot wound healing. (Reproduced with permission from [350])





**Fig. 25.40** (a) At weeks of pregnancy, the patient reported falling forward on the kitchen knife she was holding. Small bowel evisceration through a 3 cm supra-umbilical wound. (b) Stab wound after repositioning the

small bowel within the peritoneal cavity. Fetal death resulted from a penetrating thoracic wound (Fig. 5.23). (Reproduced with permission from under the CC BY 4.0 Attribution License)

The dagger left in the maternal abdomen should not be removed because it compresses the wound minimizing bleeding (Fig. 25.40), reveals the stab wound path (Fig. 25.40), and helps detect all injuries during exploration.

#### 25.4.2.1 Neurogenic Shock

It develops with the blockade of the sympathetic autonomic function by the cord injury, whether blunt or, more commonly, penetrating abdominal trauma. It is characterized by parasympathetic effects: hypotension and bradycardia with decreased cardiac output, warm, dry skin leading to heat loss, and hypothermia, leading to further bradycardia and fetal distress. This clinical picture can obscure the typical signs of hypovolemia, such as tachycardia and cold, clammy skin. Therefore, neurologic status should be obtained in any patient with abdominal trauma to exclude spinal cord injury. Neurogenic shock can be anticipated to last from 1 to 3 weeks.

#### 25.4.3 Diagnosis

Minor trauma (including minor bruising, lacerations, or contusions) may not be associated with an increased risk of placental abruption or adverse pregnancy outcomes compared to the general pregnant population. KB tests, fibrinogen levels, and coagulation studies should not be performed in this patient population to predict placental abruption or adverse events [200].

In the absence of maternal injury or any other clinically concerning signs, adopting a practice of a physical exam, brief fetal well-being assessment, and patient counseling on the warning signs and symptoms of placental abruption is an appropriate strategy for  $\geq 24$  gestational weeks presenting after minor trauma [200].

### 25.4.3.1 Laboratory Findings

After severe trauma in a pregnant woman, complete blood count, blood type, and Rh status should be determined. Additional blood tests may be indicated in patients with more severe injuries.

#### Kleihauer-Betke Test

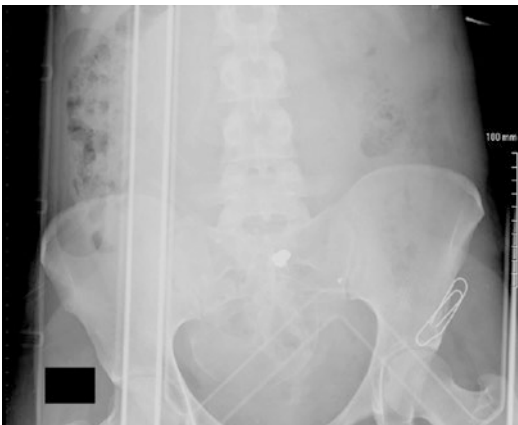
See Sect. 25.3.6.5.

#### Toxicology

In urban medical centers, 13% of pregnant patients admitted for trauma have detectable levels of alcohol, and 12% have positive toxicology screening results [45]. Therefore, alcohol levels and toxicology should be obtained during the diagnostic workup.

### 25.4.3.2 Plain Abdominal X-ray

A plain abdominal X-ray can reveal both maternal and fetal injuries. Pneumoperitoneum means injury to shallow maternal viscera. Also, bullets or fragments (Figs. 25.41 and 25.42) can be precisely located on anteroposterior and laterolateral images. If the mother is operated on and not all fragments are extracted, or the mother is treated conservatively, babygram is mandatory to check for the retained metal parts within the fetus (see Chap. 5).



**Fig. 25.41** Abdominal gunshot wound at 26 weeks of pregnancy. The white element indicates a projectile near the fetal head. (Reproduced with permission from [351])

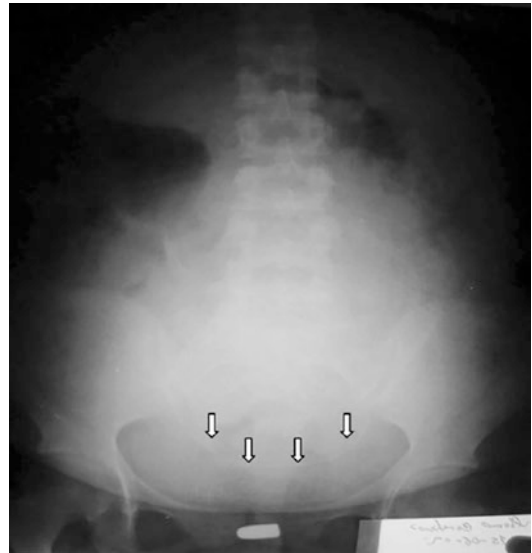
### 25.4.3.3 Transabdominal Ultrasound

#### Maternal Status

US misses 50–80% of placental abruptions [65, 67, 172] but rapidly and safely determines FHT, placental location, gestational age, and amniotic fluid index [22]. The US is helpful with maternal tachycardia, when the fetal and maternal heart rates may be difficult to distinguish with Doppler. Most obstetric US results obtained after trauma are normal [22, 40, 65, 66, 149]. Few fetuses survive after US detection of fetal trauma (Fig. 25.43) [22, 40, 65, 66, 149]. The benefit of a fetal biophysical profile after blunt trauma is unknown because it was not despite maternal injury severity [149]. The accuracy of US greatly depends on operator experience and maternal body habitus. Maternal pulsation can mimic fetal bradycardia or cause fetal movement, leading to unnecessary emergency deliveries in cases of fetal demise. The US is commonly used to reassure the mother after noncatastrophic trauma.

#### Obstetric Status

*Traumatic anhydramnios* may be caused by a leak due to the rupture of membranes with vagi-



**Fig. 25.42** Bullet inside the uterine cavity and the fetal head in vertex position. (Reproduced with permission from [350])



**Fig. 25.43** Sonogram at 25 weeks of pregnancy after a self-inflicted abdominal stab wound shows an axial section of the fetal abdomen (*inferior*) with a blood clot in the amniotic cavity encasing the umbilical cord and upper fetal surface. (Reproduced with permission from [352])

nal drainage or into the peritoneal cavity with penetrating wounds of the uterus. The latter is suspected by free fluid in the abdomen and pelvis. A fetal anomaly scan can largely exclude congenital renal tract abnormalities. Doppler flow measurements of the umbilical artery may reveal high placental resistance associated with intrauterine growth retardation [353]. Oligo- or anhydramnios in this setting would raise suspicion of placental insufficiency.

#### 25.4.3.4 Abdominal CT

It is used when the US is not diagnostic and unequivocal. Findings are similar to CT findings in maternal blunt abdominal trauma (see Sect. 25.3.7.5).

#### 25.4.3.5 Peritoneal Lavage

Diagnostic peritoneal lavage was used more in the conservative management of stable lower abdominal penetrating injury during pregnancy before modern imaging techniques [24, 54, 70, 108, 354].

### 25.4.4 Treatment

#### 25.4.4.1 Perioperative Management

See Chap. 2.

### Tetanus Prophylaxis

Tetanus is a rare, potentially fatal disease caused by the anaerobe *Clostridium tetani*. Wounds that are crushed, devitalized, or contaminated with dirt or rust are tetanus prone. Open fractures, punctures, and abscesses are also associated, but the severity of the wound does not determine the risk. All wounds should be cleaned and debrided if necessary. Tetanus toxoid should be given if the last booster was 10 years prior. If a vaccination history is unknown, tetanus toxoid can be considered when convenient. If the last immunization was >10 years ago, tetanus immune globulin should be given. The tetanus toxoid dose is 5 IU im., while tetanus immune globulin prophylaxis dosing is 250 or 500 units im. (in the opposite extremity to tetanus toxoid) [108]. Pregnancy has no immunosuppressive effect on the mothers' responses to tetanus toxoid [355].

To ensure protection against maternal and neonatal tetanus, pregnant women who have never been vaccinated against tetanus should begin the three-vaccination series containing tetanus and reduced diphtheria toxoids during pregnancy. The recommended schedule for this vaccine series is at 0 weeks, 4 weeks, and 6–12 months. The Tdap vaccine should replace one dose of Td, preferably given between 27 weeks and 36 weeks of gestation [356].

Previous maternal immunization or maternal prophylaxis induces fetal immunization against tetanus (see Chap. 5).

### Rho(D) Immune Globulin

See Sect. 25.3.6.5.

### Spinal Cord Injury

Gunshot wounds to pregnant women, especially when multiple, can result in acute spinal cord injury and penetrating abdominal trauma. Some issues are relevant to the management of the pregnant patient with spinal cord injury with fetal survival: (1) immediate measures; (2) neurogenic shock; (3) anesthetic aspects (see Chap. 2); and (4) labor management.

### Immediate Measures

General resuscitation measures included intravascular volume assessment and maintenance, stabilization of the neck, and airway maintenance (by the jaw thrust technique rather than the head tilt/chin lift maneuver). Nasal intubation may be required if in need of assisted ventilation (*American College of Surgeons, Committee on Trauma*, 1993); electronic fetal heart monitoring provides an excellent means of assessing the maternal hemodynamic status and fetal well-being. In cases of multiple injuries, it is prudent to rule out internal bleeding by peritoneal lavage with an open technique in late pregnancy or an angiogram. The peripheral neurological deficit could be due to spinal cord compression by the edema or partial/complete transection. IV methylprednisolone within 8 h of the injury as a bolus of 30 mg/kg is followed by 5.4 mg/kg for 23 h. This is associated with significant improvement in motor and sensory function 6 months after the insult [357].

### Neurogenic Shock

See Sect 25.4.2.1 for the clinical presentation of neurogenic shock from acute spinal cord injury. Management includes fluid replacement guided by central vascular monitoring and positive inotropic agents such as dopamine and dobutamine (1–5 mg/kg/min) to enhance cardiac output, perfusion pressure, and renal perfusion. There is animal evidence of the adverse effects of these drugs on the fetus, but in previous reports, these were not observed in humans with long-term use [358, 359]. Pulmonary complications of the involvement of the chest musculature by the neurological deficit are due to the restrictive effect of the pregnant uterus on the diaphragm and inadequate secretion clearance, iatrogenic pulmonary edema, malnutrition-related hypoproteinemia, and prolonged periods of hypotension that can all lead to the development of pulmonary stasis, infection, and ARDS [359].

### Pneumothorax/Hemothorax

If a thoracostomy tube is indicated, it should be placed 1–2 intercostal spaces above the usual fifth intercostal space landmark to avoid abdominal placement [26].

#### 25.4.4.2 Gunshot Wounds

##### Historical Perspective

In 1941, Bost [360] indicated that the injured gravid uterus should be emptied by CS, at almost any stage of pregnancy, especially near-term, irrespective of the fetal viability. Their rationale was to avert the possibility of a UR with labor and spare the injured patients from the additional heavy physical strain of labor and delivery during the early postoperative period. Eckerling and Teaff, in 1950 [361], confirmed these findings. The bombing of the civilian population during the siege of Jerusalem (1948) afforded them a rare opportunity of handling several cases of abdominal wounds in the late months of pregnancy.

##### Nonoperative Treatment

The practice of mandatory exploration was derived from military experience during World War II. Mandatory explorative laparotomy for all gunshot wounds to the abdomen in the general population was challenged first by Shaftan in 1960 with the selective surgical management of civilian injuries [362]. Consequently, the nonoperative approach has been neither universally accepted nor uniformly applied. The reappraisal of selective surgical management in 1980 was by Iliya et al. [363] and then Muckart [364]. Accumulating data suggest a more selective approach [70, 340, 354, 365], although high-velocity gunshot wounds to the abdomen universally require exploratory laparotomy.

Nonoperative management may apply when the entry wound is below the uterine fundus [340, 363, 365]. For upper abdominal wounds, diaphragmatic lacerations must be ruled out [354]. By displacing the bowel superiorly and posteriorly, pregnancy markedly reduces the risk of bowel injury in the lower abdomen. However, careful patient selection is critical to the success of any suggested nonoperative management. Iliya et al. [363] found a low incidence of life-threatening injury in pregnant patients and proposed the following criteria for conservative management:

- A fetus is dead,
- Entrance wound is below the level of the fundus,
- The bullet is radiographically shown to be in the uterus,
- Maternal evaluation is reassuring,
- Hematuria or rectorrhagia must be absent.

Broad-spectrum antibiotics prevent streptococcal bacteremia or clostridial myositis. Maternal surveillance requires intensive care unit monitoring, close nursing care, repeated physician examinations, and continuous fetal monitoring.

The nonoperative management of pregnant women exposed to trauma is based on various physiologic and anatomical alterations during pregnancy. A pregnant woman with physiologic hypervolemia can tolerate excessive blood loss before the deterioration of vital signs. Thus, the slightest change in vital signs may indicate impending fulminant hemodynamic decompensation. To minimize the supine hypotensive syndrome, the pregnant woman over 20 weeks of gestation should be maintained in the left decubitus position during observation. On the other hand, because the uterus is not a vital organ, maternal hemodynamic stability is maintained at the expense of uterine perfusion. As a result, the fetal circulation may suffer long before the maternal circu-

lation, and therefore late-onset fetal distress may be the earliest sign of maternal decompensation [337].

#### Medications

Regular contractions may signify placental abruption. Administration of tocolytics could compromise the fetus by delaying the diagnosis of placental abruption and consequently delaying delivery [Evidence level B] [65, 149].

#### Surgical Treatment

Kobak and Hurwitz, in 1954, recommended that all pregnant patients with a gunshot wound to the abdomen proceed to immediate laparotomy [366]. Since it is impossible to know the intra-abdominal path of a high-energy projectile, mid-line laparotomy is recommended. The signs for surgical intervention in the general population include peritoneal irritation, a positive abdominal tap, persistent unexplained maternal shock, hematemesis or rectorrhagia, and the radiologic signs of pneumoperitoneum. With this suggested approach, 12–40% of laparotomies performed for penetrating abdominal trauma were nontherapeutic and could be avoided if properly identified [279, 362].

Exploration of the maternal abdomen due to a maternal abdominal gunshot wound does not mandate CS. Indications for associated emergency CS are [367]:

- Surgical,
- Pregnant uterus mechanically limits exploration or surgical repair,
- Fetal,
- Hemorrhage,
- Interference with the fetal-maternal exchange,
- Infection.

Vaginal delivery, even in the immediate postoperative period, does not have a deleterious effect on the mother [361, 366, 368].

Metal parts should be handled with plastic gloves and removed by forceps wrapped with gauze bandages so as not to prevent ballistic investigation due to additional marks and deformation of the metal.



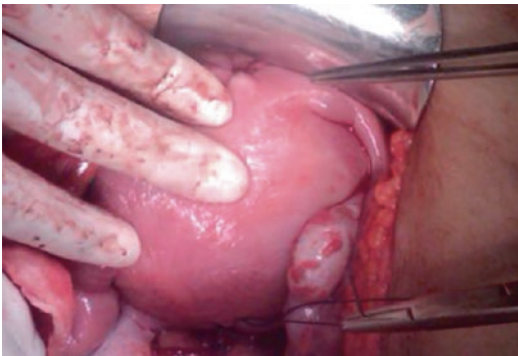
### Uterine Injury

There are three reasons for uterine exploration with a uterine gunshot wound, especially in only an entrance wound is found:

- Search for fetal injuries,
- Search for material for ballistic investigation,
- Removal of all foreign material to minimize the risk of intrauterine infection.

If the fetus is dead or previable and the uterine damage is not extensive, the uterus may be sutured, and a vaginal delivery allowed [339, 361, 366]. If the fetus is alive and viable and the uterine damage is not extensive, uterine wound repair and CS are indicated to explore potentially correctable fetal injuries. Extensive uterine damage or uncontrollable hemorrhage indicates CS and hysterectomy if the uterus is severely damaged or bleeding uncontrollably.

The uterus can complete normal labor if the wound is small and well repaired, without danger of UR (Fig. 25.44). Given its inherent elasticity, the uterine muscular wall is relatively resistant to the cavitation and stretching produced by missiles, making damage minimal and debridement



**Fig. 25.44** The surgical instruments point to the right anterolateral penetrating wound and the left posterolateral exit gunshot wound of the uterus. The bullet went through the fetal head and thorax resulting in fetal death (See Fig. 5.22). (Reproduced with permission from [369] under the CC Attribution License)

unnecessary [370]. The previous practice of mandatory debridement of military wounds was based on the observation that it reduced the risks of streptococcal bacteremia and clostridial myositis. However, with the introduction of antibiotics, this rule has been eliminated [371]. See Chap. 4 for operative principles on a gravid uterus to minimize uterine contractions.

### Obstetric Management

Wounded patients almost always well tolerate spontaneous or induced labor [350]. On the other hand, if the fetus is viable (i.e.,  $\geq 28$  weeks or  $\geq 1000$  g) and alive, emergent CS is the treatment of choice [366, 368, 372]. Emergent CS of viable fetuses that survive the initial injury after maternal stabilization (1) reduces the risk of delayed intrauterine death from occult trauma to the fetus or placental bed [373], (2) confirms placental bleeding, and (3) defines maternal injury that necessitates laparotomy [374]. After CS, the baby should be examined and all injuries noted, and fetal injuries treated if possible (see Chap. 5).

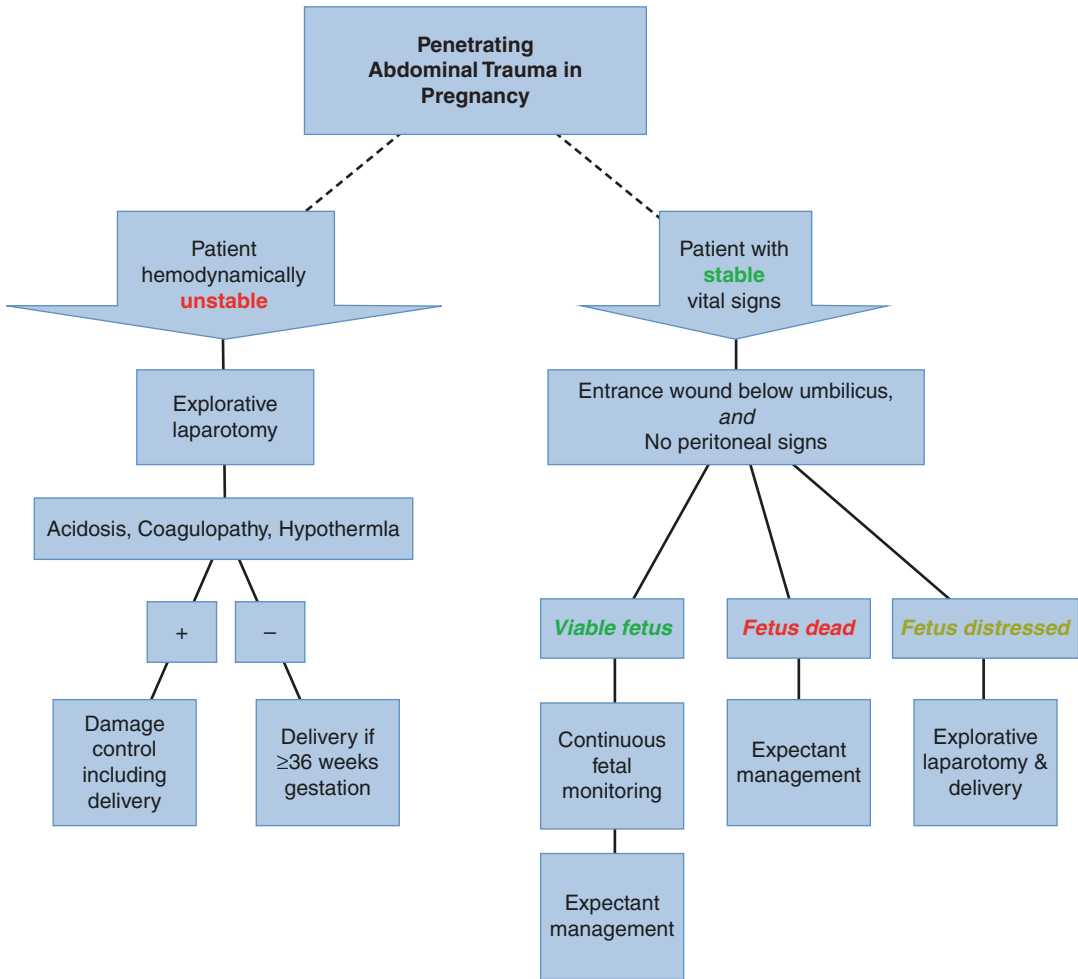
Without maternal indication for laparotomy, the preterm delivery of a live fetus with no evidence of acute distress or injuries exposes it to the risks and complications of prematurity. The US determines the need for immediate delivery [66]. With a maternal indication for laparotomy with significant damage to the uterus, CS (with hysterectomy) is recommended because of possible fetal death or significant fetal injuries that could be treated.

### Spinal Cord Injury

These patients may have painless contractions and painless cervical dilatation, which, if missed, may result in an unattended delivery and autonomic hyperreflexia. The patient should be taught self-monitoring for contractions by palpation; regular tocodynamometry and periodic cervical examinations are integral to the management.

Labor is usually rapid and often painless. The use of forceps to shorten the second stage and thus decrease the risk of autonomic hyperreflexia has been advocated [375].

The mode of delivery is influenced by the usual obstetric factors, the site and stability of the



**Fig. 25.45** Treatment algorithm for *penetrating* maternal abdominal trauma in pregnancy. (Reproduced with permission from [376] under the CC Attribution License)

lesion, the presence or absence of pelvic fractures, and the impact of pregnancy on appropriate monitoring and care.

There has been no reported increased incidence of third-stage problems or postpartum hemorrhage. Anemia, poor tissue perfusion, and lack of sensation may increase perineal or ischial abscesses [375].

#### 25.4.4.3 Stab Wounds

##### Conservative Management

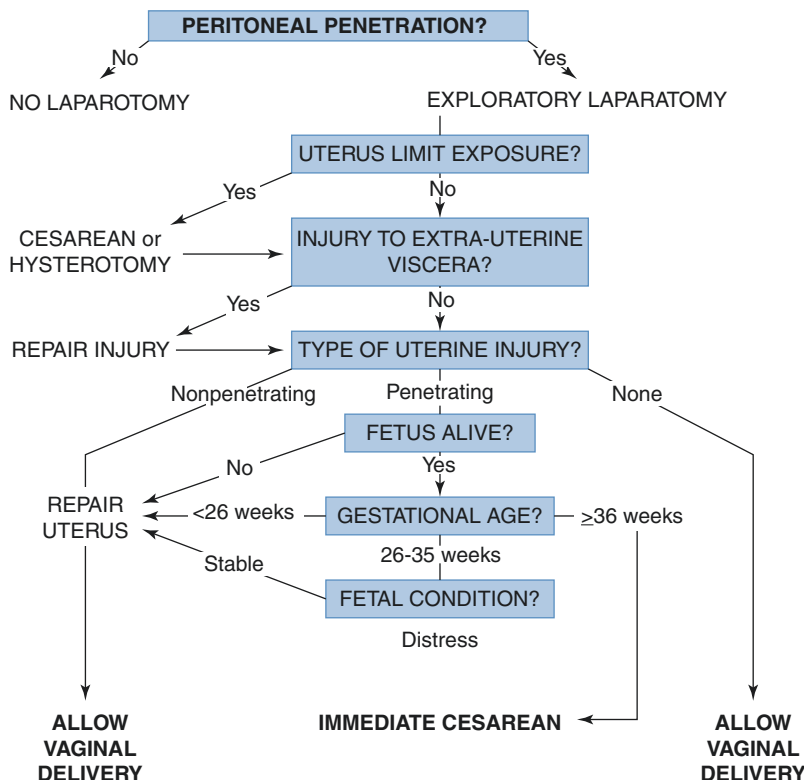
Most stab wounds without maternal hard signs, such as hypotension, evisceration, hemorrhage, or peritonitis, can be managed nonoperatively

(Fig. 25.45). In a hemodynamically stable patient, wounds should be explored under local anesthesia. If the fascia is not severed and the examining finger cannot touch intra-abdominal organs, there is no indication for abdominal exploration. During conservative/observational treatment, serial examinations of the mother and continuous external fetal monitoring are mandatory (see “Obstetric Management”).

##### Surgical Treatment

Exploration is indicated if the fascia is severed or the finger can reach intraperitoneal space. Diagnostic laparoscopy or laparotomy reveals potential intra-abdominal injuries from a low-

**Fig. 25.46** Algorithm for the management of abdominal stab wounds in pregnancy [354]



velocity stab wound. The decision to proceed with surgical exploration depends on the location of the injury, uterine size, and maternal and fetal vital signs [377].

Surgical exploration for an abdominal penetrating wound is not an absolute indication of fetal removal from an uninjured uterus. The performance of a CS significantly increases blood loss and operative time. The risk of precipitating labor after explorative laparotomy is negligible with proper care [365]. Emptying an uninjured uterus is justified only if the uterine size limits adequate abdominal exploration, repair of extra-uterine injuries, or in the presence of nonreassuring fetal status (Fig. 25.46). CS may have beneficial effects on maternal resuscitation due to eliminating the low-resistance uteroplacental circulation [24, 43]. In patients with fetal death, it is advisable to afford delivery by labor induction rather than uterine evacuation at laparotomy [70, 354, 365]. In the rare occurrence of patients in the perimortem state with a viable fetus, perimortem CS should be considered (see Sect. 25.3.7.4).

### Obstetric Management

The third-trimester fetuses subjected to stabbing injuries should be delivered promptly [378]. In contrast, injuries that penetrate the uterus may be managed with the fetus left in utero if there is no evidence of fetal distress or amnionitis [346].

Without maternal indication for laparotomy, the preterm delivery of a live fetus with no evidence of acute distress or injuries may expose it to the risks and complications of prematurity. The US and CTG determine the need for immediate delivery [66]. With indication for maternal laparotomy and significant uterine damage, CS or hysterectomy is recommended because some fetal injuries could be potentially treated.

Although perforation of the uterus near-term may require CS for fetal indications, in most cases, conservative management of uterine

wounds is acceptable [42, 379]. This usually involves simple repair of uterine lacerations with subsequent vaginal delivery. Penetrating uterine injury could be repaired even with fetal death and vaginal delivery induced later [176] only if the preoperative US or exploration excludes placental injury with abruption.

In the 1940s and 1950s, it was categorically stated that the injured gravid uterus must be emptied by CS, irrespective of fetal viability [360, 361]. Fortunately, these recommendations are not valid today.

**Brief observation** (4–6 h external fetal monitoring) is indicated when:

- Maternal trauma is minor,
- Mother is hemodynamically stable,
- Primary evaluation negative,
- FAST-US negative for intra-abdominal fluid,
- No obstetric complaints,
- <6 contractions per hour,
- Class I FHR pattern,
- Normal examination and laboratory data.

**Prolonged observation** (24–48 h EFM) is indicated with:

- Multiple or severe maternal injuries,
- Hemodynamically unstable mother,
- Obstetric symptoms (bleeding, ROM),
- >6 contractions per hour during the first 4–6 h,
- Abnormal FHR pattern or deceleration on CTG,
- Abnormal examination (e.g., fundal tenderness),
- Abnormal laboratory data (e.g., +KB, abnormal fibrinogen).

#### 25.4.4.4 Fetal Injury

See Chap. 5.

### 25.4.5 Prognosis

Emergency CS performed at >25 weeks of gestation following maternal trauma is associated with 72% maternal survival [273].

#### 25.4.5.1 Gunshot Wounds

Because the mortality rate in the general population is proportional to the number of organs involved [380], the absence of maternal death among more than 100 pregnant patients with gunshot abdominal wounds after 1912 [70, 340, 354, 365, 373, 381] indicates the protective effect of the gravid uterus. From 1845 to 1954, 33 gunshot wounds to the pregnant uterus were reported, with a maternal mortality of 9% [366]. Associated gunshot wounds to the pregnant uterus occur in 24–38% [42, 339, 366]. The maternal mortality rate is 3.9–10.5% [329, 334, 382], but half of these were due to severe head injury [28, 124, 327, 329, 334, 382], and all occurred before 1912.

The routine emergency laparotomy in the general population carries a morbidity of 8–33% [383, 384]. This is primarily due to pulmonary complications, wound infection and dehiscence, small-bowel obstruction, and iatrogenic complications. The effects may be accentuated in the pregnant woman, as physiologic ileus and diminished gastric emptying increase the risk of pulmonary complications secondary to lung aspiration during unplanned emergency surgery. Also, laparotomy wounds in advanced pregnancy can negatively impact vaginal labor and increase the possibility of a postoperative hernia.

The penetrating trauma group has a longer hospital stay ( $7 \pm 9$  vs.  $4 \pm 8$ ) than the blunt trauma group [334]. Bowel perforation does not carry higher mortality because all patients underwent laparotomy with repaired bowel lesions.

#### 25.4.5.2 Stab Wounds

Stab wounds have a better maternal prognosis due to the absence of shock waves, the ability of visceral organs to slide away from the advancing knife blade, and the protective shield of the uterus. Until 2010, maternal survival was  $\approx 100\%$ ,

and mortality rose with stab wounds to several body parts [346]. Similar maternal survival is confirmed until 2019 [10].

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**Abstract**

Although rare, these conditions present uncommon causes of bleeding during pregnancy. These are spontaneous liver rupture, peptic ulcer bleeding, and inferior epigastric artery bleeding. Bleeding from peptic ulcers and the inferior epigastric artery is commonly treated conservatively; ulcers with gastros-copy and inferior epigastric artery bleeding with percutaneous embolization. On the contrary spontaneous liver rupture due to HELLP syndrome is a life-threatening condition with high maternal and fetal mortality. Early recognition of the underlying cause before liver rupture or early surgical cessation of bleeding with the simultaneous Cesarean delivery of viable fetus contribute to improved maternal and fetal outcomes. Additional conditions included are gastrointestinal-genital communications. In the nonpregnant population, these conditions rarely require emergent surgical intervention. Deleterious fetal consequences are common in pregnancy due to the communication with the gravid uterus and the potential to cause an intra-amniotic infection. Therefore, these conditions represent a true emergency during pregnancy and should be treated surgically in consultation with an obstetrician to determine the need for delivery.

**26.1 Spontaneous Liver Rupture**

*Very exceptionally lesions of the liver are observed as the result of violent muscular exertion, as in the course of parturition or epileptic seizures. In such cases, it is usually necessary to assume a diminished resistance of the organ as a necessary condition.*

(Allesandri, 1927 [1])

**26.1.1 Historical Perspective**

Spontaneous liver rupture from insignificant or no trauma has been noted for two centuries. Vesalius reported the first case at some undetermined date. Andral, in 1829, sketchily reported two cases of complicating lesions which may have been gummata or carcinomas. In many of the earliest cases, there is some possibility that gastric hemorrhage, secondary to liver disease, may have been mistaken for the actual rupture of the liver. Thus, as reported by Latour, a case quoted in *Paris Medical*, in 1847, by Fauconneau and Dufresne was undoubtedly such an instance. John Abercrombie reported a case of ruptured liver complicating pregnancy in 1844 [2]. It was a case of a 35-year-old woman who, to obtain relief from “gastrodynia,” took recourse placing a silk handkerchief around her body and pulling it tight to give her relief. On this occasion, a servant pulled the handkerchief so tightly that *it made me*

*fearsome injury under existing circumstances.* The author, therefore, begged for its removal and prescribed a draft composed of calcined magnesia, Liquor Opii Sedativus, Spt. ether, sulfur, and Aq. cinnamomi, to be taken immediately and ordered hot fomentations to the epigastrium. The pain gradually abated. A few hours later, labor was followed by the successful breech delivery. Some 50 min after the expulsion of the placenta, the patient collapsed. Hemorrhage was suspected, but there was no evidence of its coming from the birth canal. Several famous physicians and surgeons were consulted, but the patient died 26 h after delivery. A postmortem examination revealed about two pounds of blood in the abdomen and two lacerations in the liver, about an inch apart. The liver itself presented a mottled appearance throughout and was unusually soft. The bleeding came from a torn branch of the portal vein. John Abercrombie believed that the tight bandaging caused damage to the liver but that bleeding did not occur until the pressure of the gravid uterus on the upper abdomen had been removed. He also put forward an alternative suggestion that hemorrhage took place in a liver that was already so diseased that the muscular compressions of labor readily injured it.

Devic and Beriel, in 1906, reviewed the literature on spontaneous liver rupture and coined the term *apoplexie hepaticque* [3]. Rademaker collected 28 cases in the general population and found multiple causes other than violent muscular effort. Associated disease or minor trauma was present in 25/28 cases [4]. It is no wonder that Sciacca concluded that when the liver ruptures with minimal cause, the parenchyma is probably not normal [5].

Alessandri claims that liver rupture may occur due to violent muscular activity during parturition or epileptic seizures. However, he gives no case report or reference to support his views. Rademaker suggested that sudden death during eclampsia may sometimes be due to a ruptured liver [4]. Case by Links, in 1946, during the fourth month of pregnancy, describes an unknown cause of liver damage. He suggests that it may have been due to transient hypertension. Burton-Brown and Shepherd described a hepatic rupture

from trauma produced by the violent contraction of the diaphragm and abdominal muscles during labor, presenting 17 h after parturition [6]. However, toxemia was evident in the raised blood pressure and albuminuria.

### 26.1.2 Incidence

Spontaneous liver bleeding during pregnancy is uncommon and primarily associated with preeclampsia, eclampsia, or HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count) [7, 8]. In 1982, Weinstein introduced the acronym HELLP to describe a syndrome observed in severe preeclampsia consisting of hemolysis, elevated liver function tests, and low platelet counts [9]. The subcapsular hepatic hematoma formation with capsular rupture in pregnancies varies from 1/30,863 to 1/250,000 deliveries [10–12]. Hepatic rupture in patients with HELLP syndrome is 0.4–1.8% [13, 14]. However, a spontaneous hepatic rupture in an uncomplicated pregnancy, without association with previous conditions, has been extremely rare [15, 16]. Until 1943, 29 cases (the case of Vesalius included) of true spontaneous liver rupture (only two in pregnancy, John Abercrombie in 1844 and Lee Rademaker in 1943) were described [4].

### 26.1.3 Etiopathogenesis

*In a traumatic rupture, the rupture is the cause of hemorrhage. In spontaneous rupture, hemorrhage is the cause of the rupture.*

(M. Mazel, 1919 [17])

“The chain of events leading to the rupture is infarct, hypervascularization at the periphery, rupture of a vessel, intrahepatic hemorrhage with resulting rupture of the tissue, and production of a subcapsular hematoma rupturing the capsule, which permits the escape of blood into the peritoneum” [17].

A liver rupture occurs mainly in the third trimester of pregnancy or within the first 24 h postpartum. Although preeclampsia is usually a disease of primiparous women, liver rupture

associated with preeclampsia occurs in multiparas in 80% [18] with an average age over 30 [8, 10, 19]. In 75% of the cases, it occupies the right liver lobe (mainly the anterior and superior wall), 11% occupies the left, and 14% are bilateral [18]. The pathogenesis of a spontaneous liver rupture as a complication of hypertensive disorders of pregnancy such as preeclampsia, eclampsia, or commonly HELLP syndrome remains unclear [9, 20, 21]. When bleeding follows delivery, a sudden decrease in intra-abdominal pressure or the stress of uterine contracture and the Valsalva maneuver may induce the rupture.

Preeclampsia includes three phenomena: (1) a significant alteration in microcirculatory flow distribution with increased blood flow heterogeneity, predominantly in patients with HELLP syndrome. These alterations were mainly characterized by an increased number of capillaries with sluggish, intermittent, or even stopped blood flow; (2) a reduction in the total capillary density; (3) an improvement in microvascular blood flow distribution with no variation in capillary densities after placental delivery in preeclampsia with HELLP syndrome [22].

Lee Rademaker proposed the pathogenesis of spontaneous liver rupture through four stages [23]. A first *hepatic ischemic stage* is related to preeclampsia or eclampsia, giving rise to small zones of liver infarction. This is due to microvascular vasospasm, fibrin deposition in the hepatic sinusoids, and periportal necrosis. Obstruction of blood flow in the sinusoid may cause liver distention. This phase is followed by a *phase of cicatrization*, tissue remodeling, and rising vascularization. Nevertheless, due to the poor tissue healing capacity associated with sustained intrahepatic hypertension and severe disorder of coagulation (HELLP syndrome is associated with increased complement activation [24]) and multiple parenchymal microhemorrhages give rise eventually to the third stage of *large hepatic hematoma* [13, 25]. Finally, the persistent and growing hepatic hematoma causes *rupture of subcapsular hepatic hematoma*, resulting in hypovolemic shock (fourth stage). However, there is no correlation between the severity of the

histologic findings of periportal hemorrhage and fibrin deposition and the clinical or laboratory findings [26].

The pathophysiology is attributed to the vasospasm due to increased concentration and sensitivity to circulating vasopressors during pregnancy. The increase centers on the vasopressors endothelin and angiotensin II due to the heterodimerization of ATI receptors with the bradykinin B2 receptors. This makes them resistant to inactivation by reactive oxygen species, leading to increased  $\text{Ca}^{2+}$  concentration and vasoconstriction, and reduced blood perfusion. This is followed by vascular lesion associated with endothelial damage, creating a proinflammatory and procoagulant status with platelet aggregation and the subsequent formation of microvascular thrombi and fibrin deposition that cause ischemia, necrosis, and finally, rupture (Fig. 26.1). The hepatic arterial circulation vasospasm with endothelial damage may lead to fibrin deposition. Vascular disruption and occult parenchymal hemorrhage ensue. Coalescence of multiple focal areas of infarction and hemorrhage may progress to overt parenchymal hemorrhage and hematoma. A subcapsular hematoma involving a large liver segment ruptures with resultant intraperitoneal hemorrhage. In some cases, a hematoma may develop and resolve, and the hepatic lesion may heal spontaneously without progressing to the syndrome of spontaneous hepatic hematomas



**Fig. 26.1** Ruptured hepatic subcapsular hematoma. (Reproduced with permission from [27])

**Table 26.1** Underlying causes of spontaneous hepatic rupture during pregnancy

|                                                 |
|-------------------------------------------------|
| Hemangioma/metastasis/hepatoma                  |
| Abdominal trauma                                |
| Infections (malaria, syphilis, amoebic abscess) |
| Hepatic tuberculosis                            |
| Hepatic sarcoidosis                             |
| Peliosis hepatis                                |
| Splanchnic artery aneurysms                     |
| Cocaine use                                     |
| Anabolic steroid therapy                        |
| Systemic amyloidosis                            |

associated with pregnancy (SHHP). Unruptured SHHP mandate close observation in the peripartum period for signs of hepatic rupture. Hemolysis results from the shearing of erythrocytes by fibrin strands deposited in the microcirculation, producing schistocytes. The syndrome also has been called microangiopathic hemolytic anemia. The histopathology of the liver in toxemia of pregnancy shows fibrin plugs or strands in the sinusoids and hepatic arterioles with resultant areas of periportal necrosis [20, 28].

The causes of spontaneous hepatic rupture during pregnancy are presented in Table 26.1.

**26.1.4 Clinical Presentation**

Patients with a spontaneous liver rupture present with right upper quadrant or epigastric pain (69.5%), hypovolemic shock (56%), nausea and vomiting (24.8%), abdominal distension, and a *Kehr’s sign*—a shoulder pain (20.5%) [12]. All preeclamptic patients with sudden-onset right upper quadrant pain had intraparenchymal or subcapsular hematomas [29]. In many cases, blurred vision accompanies upper right abdominal pain [30].

Hepatic rupture can present signs of peritonitis, and fetal heart sounds are usually deficient or absent. Hypovolemic shock within the first 24 h is mainly from excessive vaginal blood loss due to a failure of the uterus to contract after delivery of its contents. A laceration of maternal soft tissues like a cervical or vaginal tear can cause persistent vaginal blood loss with an appropriately

contracted uterus and no retained placental fragments. After excluding gynecologic causes, intraperitoneal bleeding from the digestive tract should be ruled out.

**26.1.5 Differential Diagnosis**

The clinical presentation of HELLP syndrome without hepatic hematoma/rupture is similar but less dramatic (see Sect. 16.2.4.2).

Rupture of hepatic adenoma or hepatocellular carcinoma should be suspected in patients without hypertensive disorders in pregnancy [31–33]. Hepatocellular carcinoma (HCC) in pregnancy is rare. From 1957 to 2013, less than 50 cases were reported worldwide [33]. Although rare, HCC must be considered in populations with a high prevalence of exposure to the hepatitis B virus. Approximately 10% of HCC rupture during pregnancy [33], partly due to tumor liquefaction necrosis. The long-term survival of the mother after hepatectomy is lower compared to nonpregnant patients [33].

Because a spontaneous hepatic rupture after a normal pregnancy is extremely rare, other more common causes of a postpartum acute abdomen or hypovolemic shock must be excluded. Cardiovascular instability without visible blood loss can also occur due to a traumatic laceration of the blood vessels resulting in a large vulvar, vaginal, or retroperitoneal hematoma. A large pulmonary embolism can also present with sudden cardiovascular instability without bleeding. It usually occurs after a deep venous thrombosis but can also occur primarily. The risk of embolism is 10× higher after a CS than after a vaginal delivery. Secondary postpartum hemorrhage results from vaginal blood loss occurring at least 24 h after the third stage of labor and during puerperium. The spectrum of this condition varies from inconvenient to fatal and occurs in almost 1% of vaginal deliveries. Nearly 50% have associated lower abdominal pain and uterine tenderness. The underlying cause is also an inability of the uterus to contract due to retained products of pregnancy or an intrauterine infection [34, 35].

Subcapsular hematoma of the left liver lobe in hemodynamically stable patients mimics perforated peptic ulcer [36].

### 26.1.6 Diagnosis

Because of the tendency of vague symptoms, the average delay in making the correct diagnosis of HELLP syndrome is 8 days [13]. The patient's hemodynamic status determines the type of investigation.

#### 26.1.6.1 Laboratory Findings

HELLP syndrome diagnosis is based on laboratory findings. Most classification systems for HELLP syndrome are based on platelet count. The *Mississippi 3-class classification* is based on the lowest observed maternal platelet count: class 1 HELLP syndrome features severe thrombocytopenia with a platelet number  $\leq 50,000/\text{mL}$ ; class 2 HELLP syndrome features moderate thrombocytopenia with a platelet number of  $50,000/\text{mL}$ – $100,000/\text{mL}$ ; and class 3 HELLP syndrome features mild thrombocytopenia with a platelet number of  $100,000/\text{mL}$ – $150,000/\text{mL}$  [14].

#### 26.1.6.2 Transabdominal Ultrasound

Transabdominal ultrasound (US) is a simple and reliable method of confirming the diagnosis of SHHP (Fig. 26.2) [20]. An urgent laparotomy is indicated with hemodynamic instability, sometimes preceded by the urgent US.

#### 26.1.6.3 Abdominal CT

With hemodynamic stability, a contrast-enhanced computed tomography (CT) is recommended. It reveals the extent of liver injury, defines the underlying hepatic disorders, and determines the treatment plan (Fig. 26.3). No correlation exists between abnormal liver imaging and the severity of hepatic function test abnormalities [39]. Only the severity of thrombocytopenia correlates with the extent of hepatic imaging findings [39]. Abdominal CT or MRI helps define the fetoplacental status (Fig. 26.4).



**Fig. 26.2** Transabdominal ultrasound shows postpartum subcapsular hematoma in a patient with preeclampsia. (Reproduced with permission from [37] under the Attribution License CC BY 4.0)



**Fig. 26.3** Native CT shows a subcapsular hematoma with a peripheral hyperdense rim corresponding to more acute bleeding. The sedimentation effect in the hematoma is an indicator of subacute bleeding. The capsule is intact. (Reproduced with permission from [38])

#### 26.1.6.4 Abdominal MRI

With hemodynamic stability, a magnetic resonance imaging (MRI) (Fig. 26.5) can be used instead of CT, with the same accuracy of quantifying liver injury, defining the underlying hepatic disorder, and determining the treatment plan. No correlation was found between abnormal liver imaging and the severity of hepatic function test abnormalities.



## 26.1.7 Treatment

### 26.1.7.1 Historical Perspective

In 1943, Lee Rademaker summarized important facts [4]:

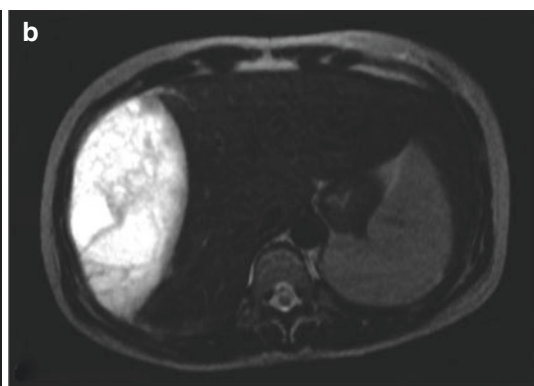
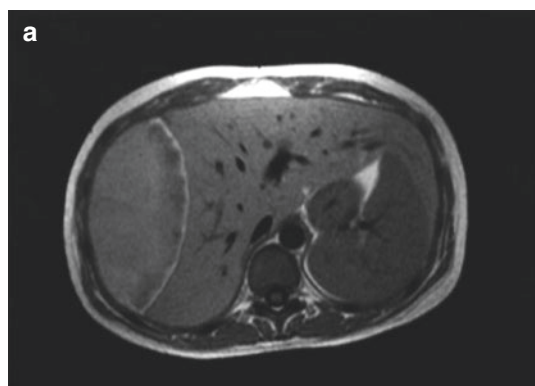


**Fig. 26.4** Coronal section of a thoracoabdominal CT shows massive hemoperitoneum with active bleeding from the placenta. (Reproduced with permission from [40] under the CC BY 4.0)

- Careful observation by the family physician; otherwise, the patient would have died within a few hours,
- *Porro procedure* was the quickest means of removal of the fetus and the uterus to prevent any further bleeding from that source,
- The death of the fetus as a result of maternal bleeding,
- Pleural effusion from the pressure of the pack on the diaphragm,
- Prompt multiple blood and plasma transfusions.

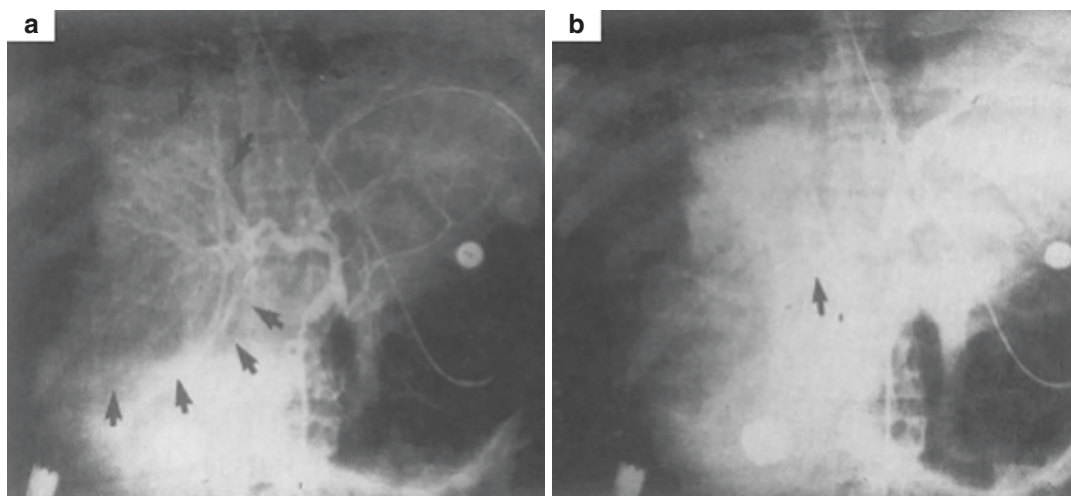
### 26.1.7.2 Conservative Treatment

Systemic anticoagulation is contraindicated. Preeclampsia-eclampsia syndrome should be treated (magnesium sulfate, antihypertensive agents, etc.). With suspicion of a hepatic lesion, control of hypertension prevents further progression and hemorrhage. Intraperitoneal rupture of the subcapsular hematoma is accompanied by bleeding and hypovolemia. Blood volume replacement is requisite, with an appropriate infusion of platelets and fresh frozen plasma. If the diagnosis is made antepartum, prompt termination of the pregnancy is mandatory, usually by emergent CS [41]. In the postpartum period, the chosen therapy mainly depends on the hemodynamic status and the severity of the liver injury. With hemodynamic stability and contained subcapsular hematoma, conservative treatment can be started. Admission to the intensive care unit for close hemodynamic monitoring is man-



**Fig. 26.5** Low-field (0.2-T) MRI shows a liquefied subcapsular liver hematoma with isointense signal intensity on (a) the T2-weighted image and (b) a hyperintense

appearance on the T1-weighted image. Typical intraleisional changes of an older hematoma. (Reproduced with permission from [38])



**Fig. 26.6** (a) Hepatic arteriogram of a patient with bleeding subcapsular hematoma. Arrows identify multiple pseudoaneurysms with bleeding. (b) Arteriogram after

embolization of the right hepatic artery (arrow). (Reproduced with permission from [45])

datory. Serial CT or US documents the expansion or rupture of the subcapsular hematoma. Surgery or hepatic artery embolization is indicated with hemodynamic instability.

Nonoperative management of unruptured SHHP is successful [20, 29, 42–44]. In some cases, 10 mg IV of dexamethasone every 12 h improves platelet recovery and shortens the evolution of HELLP syndrome.

### 26.1.7.3 Percutaneous Techniques

Hepatic artery embolization is an option for hepatic trauma, ruptured hepatoma, and spontaneous hepatic hemorrhage. Percutaneous angiographic embolization allows the most precise localization of bleeding with a high success rate (Fig. 26.6). The application depends mostly on the severity of the shock and the availability of an experienced interventional radiologist. The major advantage of embolization is its less invasiveness. Hepatic artery interruption has been well-tolerated in the general population [46]. The right and left hepatic arteries, or both, can be occluded selectively. Transient elevations in the aspartate transferase and alanine transferase levels occur. Hepatic dysfunction following hepatic artery occlusion may be accentuated in a liver with significant acute or chronic disease. If the occlusion is proximal to the origin of the cystic artery, acute

gangrenous cholecystitis may occur. Areas of focal hepatic necrosis can develop with or without secondary infection. Hypotension should be avoided after hepatic artery occlusion to maximize hepatic arterial flow. Supplemental oxygen may be administered. Hepatic perfusion through arterial collaterals may develop as little as 10 h after hepatic artery occlusion [46].

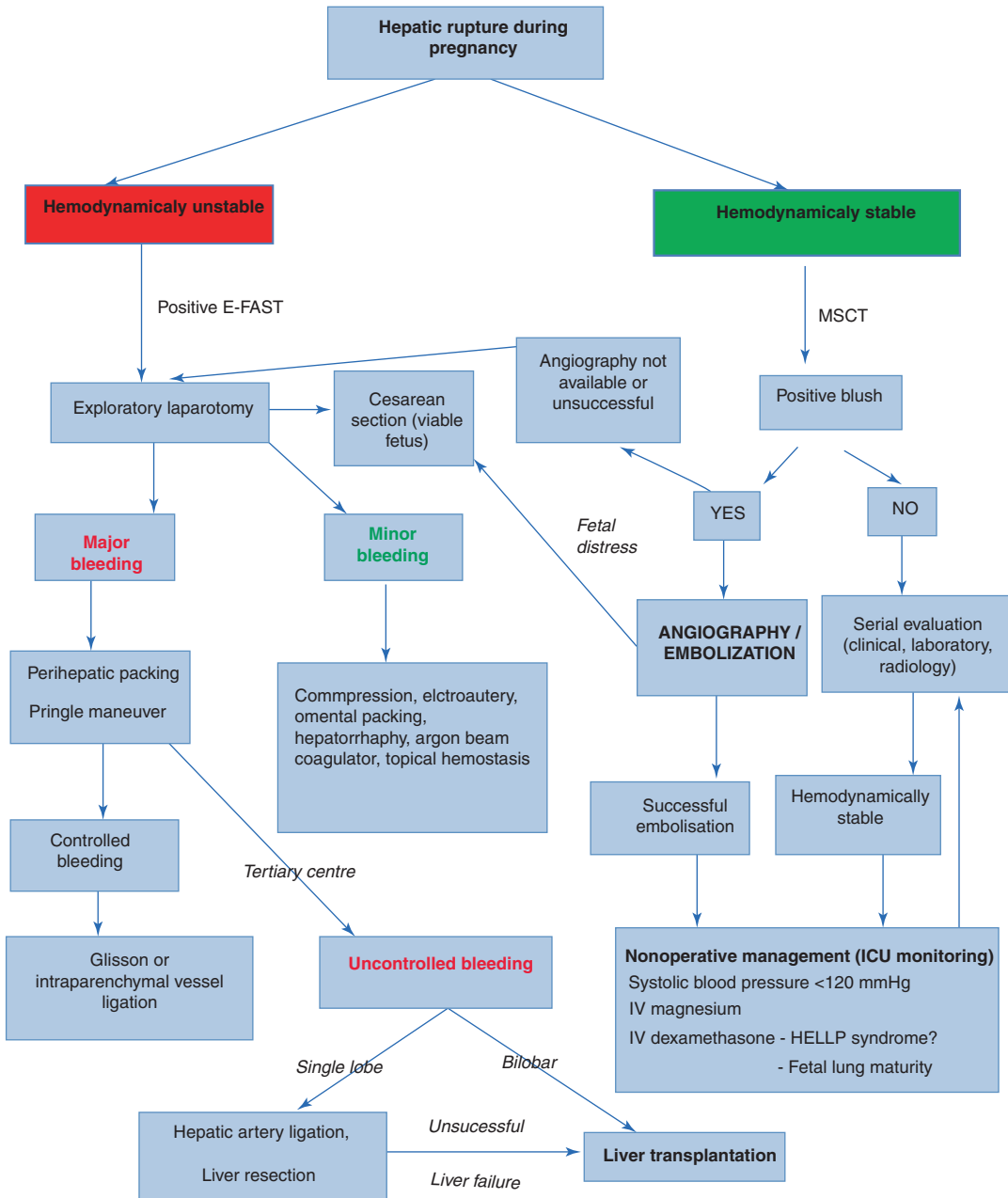
Hepatic artery embolization should be the first-line treatment in a stable woman with spontaneous hepatic rupture [27].

### 26.1.7.4 Surgical Treatment

Indications for surgery are [47]:

- Evidence of hemodynamic instability,
- Continued blood loss,
- Increasing pain,
- Expansion of the hematoma,
- Infection of the hematoma.

Surgical modalities depend on the severity of the rupture estimated on diagnostic imaging or intraoperatively (Fig. 26.7).



**Fig. 26.7** Treatment algorithm for *spontaneous* hepatic rupture in pregnancy. (Reproduced with permission from [48])

### Intraoperative Hepatic Artery Occlusion

Intraoperative hepatic artery occlusion can be the primary therapy for SHHP rather than tamponade with abdominal gauze packs [45].

### Liver Packing

The bleeding should be initially controlled with liver packing. Local measures such as topical hemostatic agents and suture ligation of surface

bleeders are of limited value, especially when dealing with bleeding from large areas of the denuded and friable liver in patients with associated clotting deficiencies. Then CS saves the baby and enables more space for definitive liver surgery if indicated.

Abdominal packing for spontaneous hepatic rupture associated with pregnancy in 1976–1990 had an 82% survival rate [11]. The recommendation was that abdominal packing should be the primary treatment for ruptured hepatic hematoma [49]. An analysis of the references cited by Smith et al. [11] reveals that in at least six reports, many patients were not treated with perihepatic packing but with local measures, including oxidized cellulose or gelfoams [9, 28, 50–52]. It is unclear if these patients exhibited the full spectrum of the syndrome, including rupture of the hepatic hematoma with life-threatening bleeding, or had contained nonbleeding hematomas.

Packing should be reserved when the diagnosis of SHHP is made at CS and in whom a Pringle maneuver incompletely controls the hepatic bleeding. In this situation, hepatic packing may be a temporary measure en route to the angiography suite. It requires a second operative procedure for removing the packs and sometimes repeated laparotomies with packing. However, if bleeding is controlled by clamping of the right, left, or common hepatic artery, hepatic arterial ligation is preferable as a definitive treatment.

### Argon Beam Coagulation

Argon beam electrocoagulation can be used alone or before packing to lessen the intensity of the bleeding. The hematoma is unroofed, and hemostasis is obtained using the argon beam coagulator [53]. The argon beam coagulator delivers a high-frequency alternating current directly to the tissue using ionized argon gas as a medium [54]. Argon gas is used because it is inert and nonflammable. The energy delivered (40–150 W) is only slightly higher than standard monopolar electrocautery (10–120 W) [54]. Heat is evenly applied to bleeding vessels and surrounding tissue, thus obtaining hemostasis without tissue contact and effectively sealing the wound. It differs from conventional spray elec-

trocautery, which requires direct contact to distribute electrical energy. This is often unevenly applied and contributes to tissue necrosis. The reduced tissue penetration depth with the argon beam coagulation minimizes tissue damage. Another shortcoming of conventional electrocautery is its relative ineffectiveness in a bloody field. The argon beam coagulator is particularly useful in situations of significant bleeding because of its ability to displace pooled blood and apply the needed energy to the underlying tissue, thus halting the source of bleeding. The eschar that also forms after argon beam coagulation is reportedly more adherent and is associated with less late rebleeding than conventional hemostatic methods [54].

### Segmental Liver Resection

Major liver resections should be avoided if possible because of the friable consistency of the liver [7]. Also, common thrombocytopenia and coagulopathy make any invasive procedure potentially treacherous.

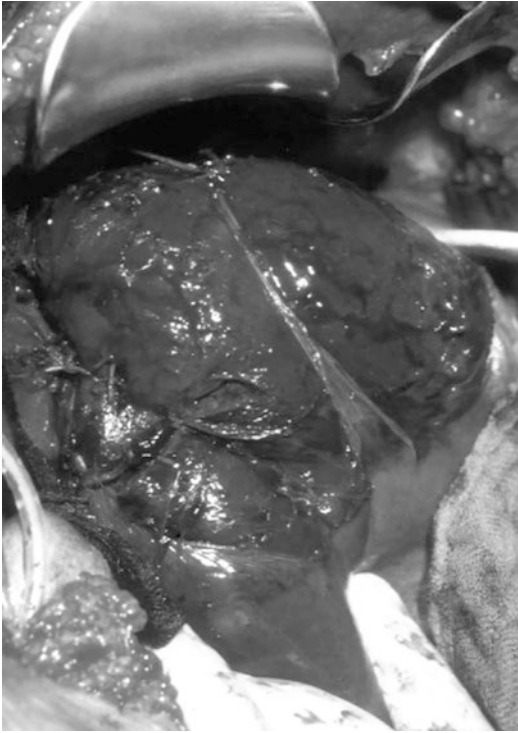
### Liver Transplantation

Erhardt et al., in 1993, made the first liver transplantation for this indication after unsuccessful perihepatic packing [55]. Three principal indications for liver transplantation as the last surgical option include (Fig. 26.8) [38, 55, 56]:

- Hemorrhage after (repeated) liver packing,
- Acute liver failure (hepatorenal syndrome ?),
- Massive destruction of both liver lobes.

### 26.1.7.5 Obstetric Management

If a rupture occurs during pregnancy, fetal delivery is the first step. A classical Pfannenstiel incision is, however, not suitable because the entire abdomen cannot be visualized unless a second upper abdominal incision is made. Therefore, a median laparotomy is recommended for Cesarean section (CS) because of better abdominal exposure, execution speed, and less blood loss [35].



**Fig. 26.8** The explanted liver with massive tears in both lobes with a maximal depth of 7 cm. Two times unsuccessful liver packing necessitated liver transplantation. (Reproduced with permission from [38])

### 26.1.8 Prognosis

Until 1943, there were 29 cases (the case of Vesalius included) of true spontaneous rupture of the liver, and only two during pregnancy (John Abercrombie in 1844, the patient died after a normal vaginal delivery; Lee Rademaker in 194 controlled the bleeding by packing, and after a stormy convalescence the patient recovered but the fetus died) [4]. More than 400 cases have been described.

#### 26.1.8.1 Maternal Outcome

Until 1899, a spontaneous hepatic rupture in the general population had 100% mortality [4]. Up to 1976, the maternal mortality rate with SHHP was 59% [8, 57, 58]. Up to 1997, maternal mortality dropped to 32% [12]. In the collected reports of

15 patients treated with hepatic artery ligation/occlusion (radiologically or surgically), the mortality was 29–37% [45, 50, 59–63]. In 1999, the survival rate of SHHP with HELLP syndrome was better with hepatic artery embolization [12]. Current maternal mortality is 17%, although there are centers with a maternal mortality of 0% [27].

#### 26.1.8.2 Fetal Outcome

Up to 1976, the fetal mortality rate during liver rupture was 62% [8, 57, 58]. Two decades later, fetal mortality was lowered to 42% [64] and recently to 25–30% [27, 65]. If the fetus survived, hypoxic-ischemic encephalopathy was common.

## 26.2 Bleeding Peptic Ulcer

### 26.2.1 Historical Perspective

LePlay, in 1905, reported the first case of bleeding from PUD in the seventh month of pregnancy at autopsy [66]. Mulsow and Brown made the first modern description of bleeding PUD in 1936 [67].

### 26.2.2 Incidence

Avery Jones, in 1947, found mild hematemesis and no ulcers in 1/10,000 women [68]. At Milwaukee County Hospital and seven other hospitals in Milwaukee from 1944 to 1953, six cases of PUD-complicating pregnancy were found in 149,491 deliveries [69]. At Whittington Hospital, from 1957 to 1960, pregnant patients represented 0.7% of all admitted patients with hematemesis and melena (JN MacCaig, 1962, personal communication). Therefore, only 0.7% of bleeding PUD occurs during pregnancy. A small number of proven cases were partly due to a reluctance to carry out radiological investigations during pregnancy before the era of endoscopy. With investigations performed after delivery, the ulcer would probably have healed.



Until 1971, 31 perforations and 32 cases of PUD hemorrhage during pregnancy were reported [70].

Due to better prevention and PUD treatment, no cases after 1998 have been published during pregnancy. The final number of cases are 40 [66, 70–94].

Bleeding PUD occurs in the late third trimester or the first days postpartum. Bleeding duodenal and gastric PUD have equal frequency during pregnancy.

### 26.2.3 Risk Factors

Pregnancy has a beneficial effect on PUD (see Chap. 22).

In 1948, four women treated with *progesterone* for threatened abortion developed bleeding PUD [84]. Severe (pre)eclampsia may be a risk factor for acute bleeding PUD (stress ulcer) [83]. Bleeding tendency characterized by thrombocytopenia, prolonged bleeding and clotting times, and intravascular coagulation is well recognized in (pre)eclampsia [95]. Gastric bleeding in patients with (pre)eclampsia could be a distinct type, with ischemia as a primary pathophysiologic phenomenon [83].

### 26.2.4 Clinical Presentation

A history suggestive of prepregnancy PUD should raise the possibility of its reactivation during gestation. Patients can have heartburn, gas indigestion, or nausea during the disease. Some patients are asymptomatic or can present with hematemesis, melena, or both. Hematemesis is often preceded by heartburn. When a significant amount of blood is lost, signs of hemorrhagic shock—pallor, cold sweat, dizziness, weakness, or disturbance of consciousness—may be present. Before the era of H<sub>2</sub>-blockers or proton pump inhibitors, episodes of bleeding recurred during the same pregnancy [96].

### 26.2.5 Differential Diagnosis

The most common causes of nonulcer hematemesis are gastric bleeding associated with (pre) eclampsia [83] or variceal bleeding. Gastric bleeding associated with (pre)eclampsia is characterized by severe projectile vomiting of blood followed by a marked decrease in blood pressure [83]. Mallory-Weiss syndrome is infrequent during pregnancy, mostly during the first trimester, usually owing to hyperemesis gravidarum. Rare cases during the third trimester have underlying pathologies such as scleroderma, acute fatty liver of pregnancy, or preeclampsia [97].

### 26.2.6 Diagnosis

A bleeding PUD is diagnosed by esophagogastroduodenoscopy (EGD). Before the era of endoscopy, PUD was diagnosed by abdominal X-rays with peroral contrast [96], but due to the ionizing radiation, it was avoided during pregnancy. Therefore, many (bleeding) PUD in pregnancy in the first half of the twentieth century were never confirmed [83].

### 26.2.7 Treatment

#### 26.2.7.1 Conservative Treatment

With potent acid suppression medications, most bleeding PUD can be treated without operation. During pregnancy, most bleedings stop with medical management [88]. Until 1953, without an intention for acid suppression, almost 100% of patients were treated medically, mostly with blood transfusions [66, 67, 79–85, 98]. After that year, nearly all cases were operated.

If needed, EGD intervention is performed. Endoscopic interventions are not contraindicated during pregnancy (see Chap. 1).

#### 26.2.7.2 Surgical Treatment

The type and location of bleeding PUD dictate the type of surgical procedure. In 1957, Vasicka et al. reported the first gastric resection with

gastroduodenostomy at 20 weeks of gestation for massive PUD bleeding. A viable infant was delivered by CS during the 33rd week [87]. After 1953 when surgical therapy started to dominate, most cases of bleeding gastric PUD were treated with gastrectomy [69, 70, 76, 89, 94, 99]. Almost all bleeding duodenal PUD were treated with sutures and, commonly, vagotomy [74, 78, 100].

## 26.2.8 Prognosis

### 26.2.8.1 Maternal Outcome

Until 1955 maternal mortality was 50% [66, 67, 69, 79–85, 98]. After 1955, and until 1998, it dropped to nearly 0% [70, 72–78, 88–91, 94, 96, 99–102].

Due to the extreme rarity of the disease, maternal mortality, in studies during the first half of the twentieth century, was also evaluated in cumulative pregnancy or puerperal deaths. MacNalty found only one death from bleeding gastric PUD in 770 puerperal deaths in 1937 [81].

### 26.2.8.2 Fetal Outcome

Fetal mortality until 1955 was 33% [66, 67, 69, 79–85, 98]. It was lower than maternal mortality because bleeding PUD started mostly during labor or early puerperium without repercussions to the fetus. After 1955 and until 1998, fetal mortality was not lowered. It was 32% [70, 72–78, 88–91, 94, 96, 99–102].



**Fig. 26.9** Charles Hilton Fagge (Hythe, Kent, England 1838–1883). (Courtesy of the Gordon Museum, King's College London). His maternal uncle, John Hilton (1804–1878), was an anatomist, surgeon, President of the *Royal College of Surgeons*, and surgeon extraordinary to Queen Victoria. His father, Charles Fagge, and his grandfather were also physicians [103]

tion, creating two stomas and reanastomosing those 2 weeks later. Charles Hilton Fagge (Fig. 26.9), at Guy's Hospital, London, published the first case in puerperium in 1876 [104]. A woman died a month after delivery, a few hours after the onset of severe abdominal symptoms. An autopsy showed thrombi in the superior mesenteric veins extending into the trunk of the portal vein nearly to the point where it breaks up into its branches. The thrombosis extended into the veins beyond the territory that was congested. No evidence of endocarditis, peritonitis, or other cause for internal strangulation was found.

## 26.3 Mesenteric Ischemia

### 26.3.1 Mesenteric Vein/Portal Vein Thrombosis

*... not everyone is aware that violent abdominal pain, ileus, and collapse may mean mesenteric vascular occlusion ...*

(Warren and Eberhard, 1935)

#### 26.3.1.1 Historical Perspective

Elliot, in 1895, first described mesenteric vein thrombosis (MVT) as a cause of intestinal infarction. He treated the infarcted bowel with resec-

#### 26.3.1.2 Incidence

MVT is rare in the general population and accounts for 0.002–0.06% of all inpatient admissions [105], 0.01% of all emergency surgical

admissions, and <1/1,000 laparotomies for the acute abdomen [106]. The venous collateral circulation of the inferior mesenteric vein is more elaborate than that of the superior. Therefore, MVT of the inferior mesenteric vein, followed by infarction of the descending colon, is exceedingly rare. The literature review of 372 cases of MVT in the general population (1911–1984) found that the condition was most common in the sixth and seventh decades of life [107], while recent series found the most common occurrence between 45 and 65 years [108, 109]. In autopsy studies, MVT is found in 0.2–2% of the general population [105] and <1% with mesenteric ischemia [105].

Until 1963, 15 cases during pregnancy and puerperium were described [110–113]. Of these, 27% resulted in abortions, 13% occurred during pregnancy, and 53% during the puerperium. After 1963, a similar number of superior MVT were published [114–123].

PVT has a similar frequency to MVT. Less than 100 cases have been published [120, 124–130]. Some patients with PVT were followed during several pregnancies [124].

26.3.1.3 Risk Factors

Virchow’s triad is responsible for the formation of every thrombus. It includes damage to the vascular endothelium, changes in the velocity and character of the local bloodstream, and changes in the constituents of the blood. MVT is uncommon and frequently associated with coagulation defects [115–117]. The maternal risk of thromboembolic episodes is increased eight times in the presence of any one of the coagulopathies [131]. The factor V Leiden mutation may be as high as 46% in patients with a history of venous thromboembolism during pregnancy [132].

MVT can be present without detectable coagulation errors and is rarely encountered in pregnancy [115, 133, 134]. This condition is attributed to the physiological hypercoagulability of pregnancy from multiple factors, including a rise in factors VII and VIII and fibrinogen and a reduction in fibrinolytic activity [133]. However, a rise in platelet count with increased platelet stickiness maximal on the 12th day of puerperium has been demonstrated [135]. Factor V mutation, protein S

**Table 26.2** Mesenteric venous thrombosis risk factors in pregnancy and puerperium [114–119, 133, 137–141]

|                                               |
|-----------------------------------------------|
| Multiple pregnancies                          |
| Hypercoagulopathies                           |
| Oral pills during pregnancy or puerperium     |
| Postoperative                                 |
| Abdominal surgery                             |
| Cesarean section                              |
| Cytomegalovirus infection                     |
| Chronic idiopathic mesenteric vein thrombosis |
| In vitro fertilization pregnancy              |
| Hemoglobinopathy                              |
| Primary (idiopathic)                          |
| Smoking                                       |
| Obesity                                       |
| β-thalassemia                                 |
| Antiphospholipid syndrome                     |
| Abnormal fibrinogen                           |
| Homocystinuria                                |
| Paroxysmal nocturnal hemoglobinuria           |
| Thrombocythemia                               |
| Abdominal trauma                              |
| Abdominal sepsis                              |
| Myeloproliferative disorders                  |
| Cancer                                        |

deficiency, and estrogen-based hormonal therapy are common [123]. Less than 50% are *primary (idiopathic)* MVT without precipitating factors [123]. In addition, the enlarging uterus compresses the inferior vena cava. The resulting increase in blood flow stasis adds to the prothrombogenic risk [115].

A specific group of MVT in pregnancy is associated with particular surgical and medical conditions, including previous abdominal surgery, bariatric surgery [136], CS, vesicoureteral reflux, and mistaken intake of oral contraceptives during pregnancy (Table 26.2). Additional risk factors include heavy smoking [137] or high BMI. The anatomic location of venous thromboembolism associated with IVF differs from that of the general population. In venous thrombosis associated with IVF, the upper extremities and neck veins are involved in 80%, whereas only 11% of deep vein thrombosis diagnosed in the general population involves the upper extremities [142]. Furthermore, 97% of upper extremity deep vein thrombosis reported during pregnancy was associated with assisted reproductive technology [143].

MVT may occur in the postpartum period, regardless of the delivery route—vaginal [144] or CS [120]. This is possible due to hypercoagulability and hemoconcentration during the first days after delivery, caused by blood loss, ranging between 500 and 1000 ml, depending on the delivery route. However, comorbidities or complications can have a greater role in developing thrombosis. It is more common in multiparas [119, 138].

Risk factors for PVT are similar to MVT (Table 26.2). The main underlying causes of PVT identified before pregnancy and in the absence of liver insufficiency were myeloproliferative neoplasm, protein S deficiency, and antiphospholipid syndrome [130]. A risk factor more common in PVT than MVT is cirrhosis. Recently, a COVID-19 infection has been recognized as a risk factor inducing a hypercoagulable state [145]. The median period from diagnosis of PVT to the first conception was 29 months (range 7–344 months) [124]. Additional MVT was present in 38%, and complete obstruction of the main portal vein in 92% [124]. A hypercoagulable state is present in 12% [146].

#### 26.3.1.4 Clinical Presentation

Clinical symptoms of *acute* MVT are variable, nonspecific, and difficult to differentiate from arterial occlusion. The hallmark of acute MVT is abdominal pain, typically described as colicky and midabdominal [147]. Initially, the pain may be mild. Initial physical findings may be entirely normal. With the progression of the disease, the pain can become quite severe but often remains out of proportion to physical signs [147]. Nausea, anorexia, vomiting, and diarrhea are common. Some patients may experience hematemesis, hematochezia, or melena [147]. Abdominal signs such as abdominal tenderness, distension, and ascites may accompany bowel ischemia [147]. The tendency toward hemoconcentration is also characteristic and probably reflects the slow progress of the disease, allowing the sequestration of extracellular fluid in the gut. The occult blood in the stools is common [148]. A digital rectal examination may show blood. With

hematemesis in acute form, splenic vein thrombosis is present, but splenic vein thrombosis is not necessarily followed by hematemesis.

*Subacute* or *chronic* MVT is usually asymptomatic due to the development of collateral vessels, but when combined with portal vein thrombosis, esophageal variceal bleeding with hematemesis may occur [109]. Most patients in the general population using oral contraception had at least 2 weeks of symptoms such as abdominal pain, discomfort, anorexia, vomiting, and change in bowel habits [149]. Sometimes the leading presentation can be spontaneous abortion or stillbirth [111].

The clinical presentation of PVT is different from MVT. Most patients present with a history of acute right hypochondrial pain that lasts from hours to several days and a fever of 38 °C [127]. The signs include tachycardia, fever, and tenderness in the upper right abdominal quadrant without peritoneal irritation [130]. Hematemesis is highly variable, from 0% [146] to 71% when esophageal varices are present [146]. Variable incidence is partly due to prepregnancy variceal bleeding treatment by endoscopic sclerotherapy or ligation [146]. Some present with an asymptomatic palpable enlarged spleen [146].

#### 26.3.1.5 Differential Diagnosis

Patients with abdominal pain may be mistaken for gastritis, peptic ulcer, acute appendicitis, or colonic diverticulitis. Diarrhea may mislead the diagnosis of enteritis. With severe abdominal pain, acute pancreatitis is often suspected. The early symptoms of MVT in a pregnant woman are often wrongfully interpreted as regular changes in pregnancy or more common pregnancy complications such as spontaneous abortion, preterm delivery, uterine rupture, or placental abruption [121, 122].

PVT can be mistaken for acute cholecystitis or HELLP syndrome.

#### 26.3.1.6 Diagnosis

Clinical diagnosis of MVT or PVT is difficult and delayed due to a lack of awareness and the absence of active signs in the early stages of the

disease. Furthermore, the early features of the disease get masked by the effects of pregnancy. Hopefully, PVT is mostly chronic, and most patients have the diagnosis before pregnancy [124, 146].

### Laboratory Findings

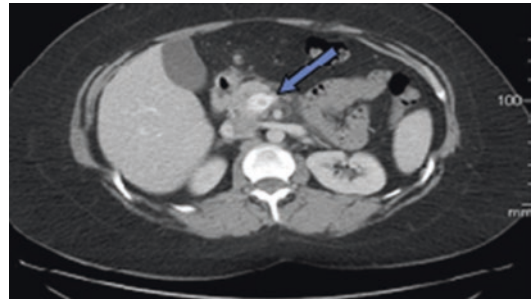
Anemia is present in 40% [146, 150]. Thrombocytopenia is common (50–62%) with splenomegaly and hypersplenism [146, 150]. Liver enzymes are mostly in the normal range [124].

### Diagnostic Imaging

A plain abdominal X-ray can be normal [123] or shows hardly visible air-fluid levels [151].

The Ultrasound (US) can show a thickening of the intestinal wall and a small amount of ascites [123]. Color Doppler US shows the absence of venous blood flow [120, 152]. With PVT, urgent transabdominal US rules out acute cholecystitis. However, it can demonstrate well-defined homogenous hyperechoic oval-shaped formation in the splenomesenteric confluence or branches of the portal vein. Color Doppler US confirms these findings by showing the margination of the colored flow in the residual lumen. Splenic and mesenteric veins should be visualized because untreated thrombosis leads to bowel ischemia. The hepatic artery shows increased compensatory flow. Collateral venous circulation should be verified or excluded because it helps to establish a definitive diagnosis. The color Doppler US features of acute MVT or PVT are:

1. The thrombosed vein usually displays an echogenic appearance (70% in the general population) [153]. The US shows a dilated vein with the loss of respiratory motions and venous distension upstream of the thrombosis. Transient ascites may be seen, denoting acute portal hypertension. Color Doppler US confirms the diagnosis by the absence of intraluminal colored flow in complete thrombosis or eccentric or margined colored flow in partial thrombosis. Also, the Doppler US demonstrates an increased compensatory flow in the hepatic



**Fig. 26.10** Abdominal CT shows a superior mesenteric vein thrombosis (blue arrow) in an IVF patient. (Reproduced with permission from [139])

artery and periportal collateral venous circulation that may develop after 1 week [153],

2. Alternatively, the thrombosed vein displays an anechoic appearance (20–30%). US may miss the thrombus, while color Doppler US demonstrates the filling defect within the venous lumen [153]. When Doppler US confirms PVT, a complete coagulation profile should be obtained.

Abdominal CT can reveal minimal thickening of the bowel wall [151]. Contrast-enhanced abdominal CT defines the location and extent of thrombosis and is a diagnostic method of choice (Fig. 26.10). MRI has no advantage over CT [109]. The angiography showed only 55% sensitivity and was not suggested as a primary diagnostic modality [109].

Often, a definitive diagnosis is made during surgical exploration, mostly for the acute abdomen. Without strangulation, volvulus, mesenteric thromboembolism, or cocaine abuse should be excluded [154].

#### 26.3.1.7 Treatment

Multidisciplinary management in the tertiary center involves hepatobiliary surgery, interventional radiology, hematology, obstetrics, and neonatology. Most importantly, the treatment depends on the stage and extent of the disease [109]. For PVT with hypersplenism, splenectomy without shunt surgery should not be performed [146].



### Anticoagulation

PVT without bowel infarction or peritonitis is treated with anticoagulation with heparin converted to LMWH, followed by warfarin after delivery [109, 151]. Due to the known preconception PVT, almost half of the patients had anticoagulation before pregnancy [124]. No patient stopped anticoagulation during pregnancy [124]. Heparin prevents the recurrence of thrombosis after intestinal resection (14% vs. 26%) [107] and is associated with lower mortality when recurrence occurs (22% vs. 59% [107]). In anticoagulated patients not undergoing surgery, most thrombosed veins will partially or entirely recanalize over time (see Sect. 2.2.3.8) [120].

Prompt treatment of PVT prevents progression to portal hypertension with the risk of variceal bleeding [129]. At first conception, 67% had esophageal varices, which had previously ruptured in more than half of these cases [124].

Response to therapy for MVT and PVT in pregnancy cannot be estimated due to the extremely small number of cases. However, color Doppler US monitoring confirms the response to treatment [120, 151, 153, 155].

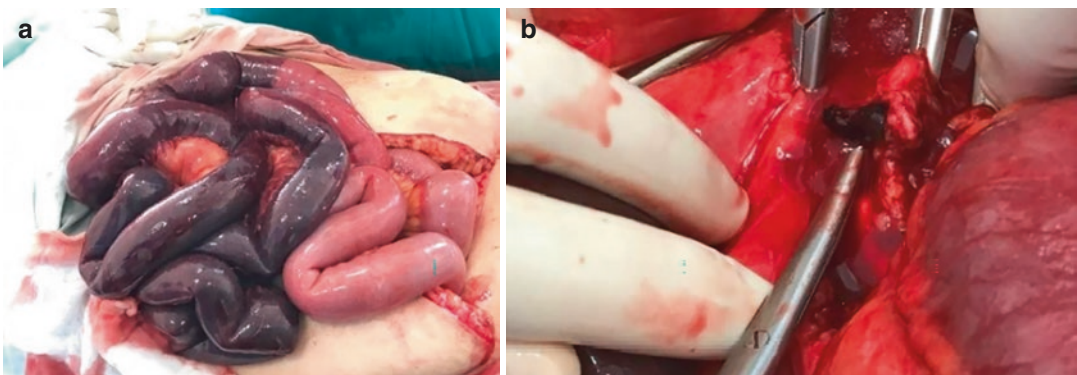
### Surgery

Explorative laparotomy is indicated when diagnostic modalities do not reveal the cause of acute abdomen or when intestinal infarction is suspected/confirmed (Fig. 26.11). First, the intestinal

obstruction should be excluded due to different pathophysiology and treatment (see Chap. 18) [156]. Consideration should be given to intra-arterial papaverine to reverse (arterial) spasms and relax the uterus preventing spontaneous abortion or preterm labor. The thrombolytic agents via operatively placed catheters and continued heparin may prevent the extension of infarction.

With segmental gangrenous segments, minimal resections should be performed to minimize the possibility of short bowel syndrome. Multiple resections with anastomoses with or without proximal stoma are recommended. Another option after multiple segmental resections is to close (potentially) viable bowel segments by stapling and the abdomen left open with vacuum-assisted closure (VAC) with 125 mmHg continuous negative pressure (see Chap. 3). The viability of the remaining bowel is assessed after 24 to 48 h [118]. Additional intestinal resection could be required at the second and third surgical looks. Eventually, after 48 h of open abdomen management, intestinal continuity should be restored. The abdominal wall should be closed or rarely laparostomy prolonged for several days (see Chap. 3).

The enlarged spleen with protein C deficiency and its gastric compression could become prominent with anemia, leucopenia, and mild-severe thrombocytopenia. Some recommend splenectomy with occasional protein C concentrate [129].



**Fig. 26.11** (a) Segmental gangrene of the small intestine without obstruction and perforation due to mesenteric vein thrombosis. (b) Thrombectomy from the branch of

the superior mesenteric vein. (Reproduced with permission from [138] under the CC Attribution License)

### Thrombectomy

The thrombectomy route is percutaneous or surgical. Surgical thrombectomy or a combination of surgical thrombectomy of MVT (Fig. 26.11) and regional heparinization have been reported. In pregnancy, thrombolytic treatment is not advocated [133].

### Obstetric Management

#### Continuation of Pregnancy

In pregnant PVT patients treated with anticoagulation on an individual basis, the rate of miscarriage and preterm birth (in 38% of deliveries) appears to be increased. However, fetal and maternal outcomes are good for most pregnancies reaching gestation week 20.

Even after several operations due to gangrenous bowel and open abdomen treatment during pregnancy, term vaginal delivery is allowed [118].

#### Mode of Delivery

With proven PVT during pregnancy, further complications during and after delivery should be prevented. Staining and bearing down during vaginal delivery result in a significant but transient portal vein pressure increase. For some, avoiding vaginal delivery should minimize the rise in portal vein pressure and reduce the possibility of variceal bleeding [129, 157].

Standard peripartum management is to stop anticoagulant therapy when contractions start or administer the last dose 24 h before labor induction. Anticoagulant therapy restarts 12–24 h after delivery if postpartum hemostasis is achieved [125].

Vaginal delivery ranges from 47 to 84 53% of deliveries [124, 146]. Postpartum bleeding did not differ between CS and vaginal delivery [124]. Half of the women required platelet transfusion in the intrapartum period due to hypersplenism resulting in thrombocytopenia [146]. Platelet transfusion is required intrapartum if the count is less than 50,000/mm<sup>3</sup>.

### 26.3.1.8 Prognosis

The mortality rate among patients with acute MVT ranges from 20 to 50% [147]. The subgroup with oral contraception (until 1977) had high mortality (50%) and morbidity rates—50% required at least two operations. Arterial thrombosis carried twice the mortality of venous thrombosis but was half as common [142].

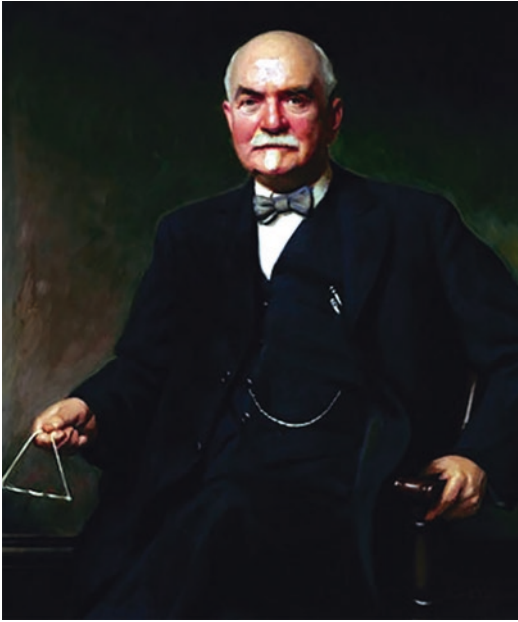
Until 1963, maternal mortality from MVT was 87%, and the two patients who survived were from the last year (1963) of the analyzed period [110, 111]. During the last several decades, maternal mortality dropped to 7% [123]. Fetal mortality from MVT, including elective abortion, has been 33% in the previous several decades [123]. An unfavorable prognosis of PVT is associated with high platelet levels, JAK mutation, and ascites [124, 125].

Maternal mortality from PVT is 0% [125, 150]. Previous early pregnancy loss is 20% [124]. The incidence of abortion, preterm deliveries, small for gestational age, and stillbirths were 20–24%, 15–19%, 13%, and 7.7%, respectively [146, 150]. Anticoagulation during pregnancy is not associated with an increased risk of pregnancy loss or maternal adverse events [125].

## 26.4 Rectus Sheath Hematoma

### 26.4.1 Historical Perspective

Rectus sheath hematoma (RSH) is an ancient disorder first accurately described by Hippocrates and mentioned by Galen. In 1925, Carey Culbertson reported two cases considering their gynecological and obstetrical significance [158]. Thomas Stephen Cullen (Fig. 26.12), in 1918, first described bluish periumbilical discoloration from ruptured ectopic pregnancy. Then Cullen and Brödel, in 1937, at Johns Hopkins Hospital, reported two cases of spontaneous RSH during pregnancy [159, 160]. Both were black patients. The resolution was uneventful in a 7-month pregnancy, while another exploration was unsuccessful.



**Fig. 26.12** Thomas Stephen Cullen (1868–1953); painting by Thomas C. Corner; oil on canvas, 48 by 40 in., 1907. (Courtesy of the Alan Mason Chesney Medical Archives of the Johns Hopkins Medical Institutions)

## 26.4.2 Anatomy

The inferior epigastric artery (IEA) arises from the external iliac artery deep into the inguinal ligament. It serves as a surgical landmark and constitutes a potential target for injury during inguinal hernia repair. The IEA divides deep to the rectus sheath into two branches: an ascending branch that anastomoses at the umbilicus, medial to the rectus sheath, with the abdominal branch (or superior epigastric artery) of the internal thoracic artery, and a descending branch that gives off obturator branches that course along the ischium and anastomose with the obturator artery and pubic branches, which in turn the course along the pubic rami and reach the pubic symphysis.

## 26.4.3 Incidence and Risk Factors

The most common causes in pregnancy are coughing (73%) and labor with blunt trauma accounting for only 8% of cases [161].

### 26.4.3.1 Spontaneous Rectus Sheath Hematoma

In the general population, 60% are on the right side, and more than 80% are in the lower quadrants [162]. Maxwell, in 1929, collected 11 cases in pregnancy [163]; 73% were during pregnancy and 27% during labor. Torpin, in 1943, analyzed 27 reported cases during pregnancy [164]. Riera et al., in 2009, collected 52 cases [165], while Humphrey et al., in 2001, collected 69 cases in English language literature [161]. The decreasing incidence of spontaneous RSH is the result of:

- Lower exposure to blunt or penetrating abdominopelvic trauma,
- Avoidance of heavy lifting,
- Less respiratory conditions due to avoidance of closed spaces and people,
- A decrease in the incidence of influenza,
- The decline of grand multiparity.

The mean gestational age of RSH was 32.4 weeks, without cases in the first trimester. The mean parity was 5.1 [161]. There is no side predilection, and bilateral RSH was always preceded by labor [161].

### 26.4.3.2 Postcesarean Section

Early reoperation rate after CS in India is 0.45–0.6% [166, 167]. In two Indian case studies with early relaparotomy after CS, RSH was found in 21–27% [166, 167]. In Western countries, this is extremely rare during pregnancy, with several reports after CS [168–170].

## 26.4.4 Mechanism of Injury

### 26.4.4.1 Direct Trauma

Direct injuries of the IEA include *blunt trauma* [169] or *penetrating abdominal wall trauma*. Distension of the abdominal wall during pregnancy causes elongation of the inferior epigastric artery. Blunt trauma to that region possibly causes further distension of the inferior epigastric artery

beyond its elastic modulus, making it prone to tears and lacerations with subsequent bleeding [171]. If delivery occurs immediately after abdominal trauma, it is unknown whether the cause is abdominal trauma or delivery with straining [163].

Iatrogenic abdominal wall trauma during interventions, including CS, paracentesis, and trocar insertion during laparoscopy, causes direct IEA injury. Injuries to the ascending branch usually occur after direct trauma to the abdominal wall, for instance, during laparoscopic surgery, subcutaneous injections, lumboperitoneal shunts, or ascites fluid aspiration. Emergency CS is a risk factor for IEA injury [166]. At CS, care during transverse cutting and suturing of the lateral extension of the rectus sheath is advised [167].

#### 26.4.4.2 Spontaneous

The condition occurs mainly in multipara and late in pregnancy. It is also found during labor, the expulsion of the placenta, and early puerperium. Usually, there was evidence of labor trauma, coughing, or a fall. Muscle degeneration from influenza or typhoid is a possible cause. Even excessive fetal movements in advanced pregnancy could cause RSH [172].

The precipitating factor in most spontaneous cases seems to be the inelasticity of the wall of an artery or vein, which prevents the vessel from accommodating itself in a movement, a cough, or a sneeze or, in or after labor, to the remarkable variations in length which the rectus muscle undergoes between extreme contraction and extreme relaxation. According to Brodel, there is only one major vessel to take care of this long muscle stretch. To avoid damage to itself, it must keep away from the muscle as far as possible and send its branches into the muscle substance so that the muscle action does not interfere with vascular freedom. The larger intramuscular arteries branch freely and form numerous anastomoses. They run at an angle varying from 60° to 90° to the axes of the muscle bundles. An occasional artery that runs parallel to the muscle bundle increases tortuosity. The arteries are less apt to tear than the veins because they are far more resistant. They lie and are so loosely embedded in

the intramuscular connective tissue that they can be pulled out quite far without injury, but not so with the veins. They are frail, of smaller caliber, and have thinner walls. Tears may be partial or complete. In a partial tear, only branches of the main vessels rupture beyond their point of entry into the muscle body, but a complete tear is apt to rupture the main trunk.

Right-sided hematomas in the general population are more common because more people are right-handed and more prone to the right-sided strain of the rectus muscle during strenuous activity. The lower quadrants are more frequently involved because of the long vascular branches, and muscle excursion during contraction without the tendinous inscriptions is greater [162]. In pregnancy, the RSH is commonly located between the pubic symphysis and the umbilicus [161]. This is similar to nonpregnant patients, with 77–94% RSH located beneath the umbilicus [173].

Rarely, the ascending branch may rupture spontaneously, primarily in patients taking anticoagulant medications after lifting heavy weights, coughing, or straining. Thus, the tearing of the branches of the epigastric vessels is a well-known cause of RSH [174].

### 26.4.5 Clinical Presentation

#### 26.4.5.1 Spontaneous Rectus Sheath Hematoma

A history of anticoagulant therapy, coughing or sneezing (60%), straining, or twisting to one side should raise a suspicion of RSH [175]. Awareness of RSH during pregnancy is important because the abdominal wall is easily overlooked as a cause of acute abdominal pain [161, 176], given the higher prevalence of other pregnancy-associated pain.

Among the clinical findings, vague premonitory discomfort at the bleeding site is common with lesser degrees of hemorrhage. Probably a great number of the RSH are small, unnoticed, and consequently unreported. In most recorded cases, the hematoma was limited to the rectus sheath, and pain and tenderness were felt over the bleeding

area. Muscle rigidity is often marked in the involved rectus, but in small hemorrhages, only a local tenseness is present. Swelling and palpable firm, nonpulsatile mass is usually confined to the affected muscle sheath. Swelling of the hematoma is limited to the rectus abdominis muscle, with its sheath not extending beyond the abdominal midline or the lateral borders of the muscle (*Romanzew's sign*). However, the posterior sheath may communicate below the arcuate line, and the mass may project across the midline or extend inferiorly and posteriorly toward the bladder. In some cases, the bleeding escaped the limits of the muscle sheath and extended into the broad ligament or ruptured into the peritoneal cavity [177].

The bleeding initially lies between the fascia transversalis and the posterior surface of the rectus muscle, spreading later to surround the muscle and ascending over the linea semilunaris between the rectus muscle and its posterior sheath sometimes downward behind the rectus. If the patient lifts her head off the pillow to contract the rectus, the mass can be felt confined to the rectus sheath and immovable. The mass is equally palpable when the patient is lying supine or partially sitting up (*Fothergill's sign*). A swollen and palpable mass is usually confined to the affected muscle sheath and severe, usually unilateral, abdominal pain aggravated by movement [178].

*Carnett's sign* is performed by first localizing the area of maximal tenderness while the patient is relaxed. While this area is being pressed, the patient is asked to raise her upper back, effectively tensing the abdominal wall. Worsening of the pain is considered a positive test [179]. In 1926, Carnett recognized that abdominal pain could be from neuralgia affecting one or more of the lower six intercostal nerves and developed a simple test to help localize the origin of symptoms to the abdominal wall [180]. For this part of the abdominal examination, the patient is asked to lift the head and shoulders from the examination table to tense the abdominal muscles. An alternative is to ask the patient to raise both legs with straight knees.

Staining of the skin and ecchymosis are common over the palpable mass (*Cullen's sign*), first described by Guthrie and Stamfey, who also

found *Grey-Turner's sign* with RSH [181]. These occur over the center of the hematoma, as a semi-circle around the umbilicus, above the pubis, or along the linea alba. The extravasated blood can pass more easily superficially around the medial border of the rectus. The pigments that produce this phenomenon may reach their destination by following the ordinary fascial planes but not by the lymphatics, as was previously believed. In RSH, ecchymosis appears after 2–5 days.

The gynecologic examination is usually normal, without vaginal bleeding or dilation of the cervix [172]. With smaller RSH, the fetal heart rate is normal and reassuring, without uterine contractions on CTG [161]. With large RSH, CTG shows fetal tachycardia, reduced variability, or fetal heart decelerations with no noticeable contractions [172].

#### 26.4.5.2 Traumatic Rectus Sheath Hematoma

Traumatic RSH includes external trauma and iatrogenic injury from surgery or interventional techniques. The presentation is the same as spontaneous RSH, but additional injuries should be excluded, especially in high-energy trauma such as motor vehicle accidents. Iatrogenic RSH is found after CS [182]. Clinical presentation depends on the severity and timing of the injury. Significant bleeding ensues with intraoperative IEA injury/transection. If the peritoneum is intact, then a large subperitoneal hematoma is found. If the peritoneum is damaged, significant bleeding into the abdominal cavity from the abdominal wall is found. If the bleeding is not observed intraoperatively, then the severity of the clinical presentation depends on the caliber of the injured artery. If IEA is damaged, symptoms and signs of significant blood loss and hemorrhagic shock will appear immediately after the operation: tachycardia, lowered blood pressure, increased pulse rate, pallor, and cold sweat. Additionally, the patient will have a distended and painful abdomen. On inspection, hematoma over the IEA is found.

In pregnant patients, it is reasonable to expect that the shape of an RSH may be slightly different from that in nonpregnant patients because of compression from the gravid uterus [161].



### 26.4.6 Differential Diagnosis

A correct initial diagnosis was made in 38–49% [161, 183]. Clinical diagnosis of spontaneous RSH is challenging because skin changes with small hematomas are invisible. Larger hematomas result in significant acute pain with peritoneal irritation mimicking intra-abdominal conditions such as acute appendicitis, diverticulitis, cholecystitis, tumors, and visceral injuries [174]. The most common incorrect diagnosis was placental abruption, followed by ovarian torsion, cyst, tumor, hemorrhage [161], uterine rupture, or degenerating uterine fibroids [176, 184]. Some incorrect diagnoses are confirmed on US because the retroperitoneal extension of hematoma mimics retroplacental hematoma, placental abruption, or uterine fibroid degeneration [185]. Normal fetal CTG should initiate the search for other causes [185]. Transaminases can be elevated due to their release from muscle trauma/destruction. This can mislead the clinician about the hepatic cause of the condition.

### 26.4.7 Diagnosis

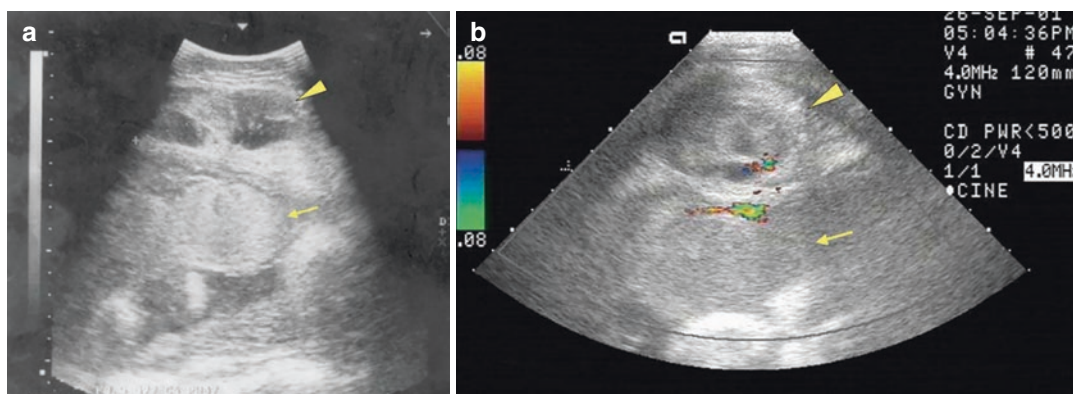
#### 26.4.7.1 Transabdominal Ultrasound

The US often shows a heterogeneous hypoechoic mass in the abdominal wall (Fig. 26.13) and is most helpful in detecting RSH [161]. Cystic

forms with thickened, irregular septa or homogeneity without septal or cystic components exist [186]. This is probably related to the age and organization of the hematoma. Greater anteroposterior diameter of the rectus abdominis muscle should be noted on the affected side. The mass is often near the uterus and appears to arise from the uterus mimicking uterine pathologies such as degenerating uterine myoma or ovarian mass [161]. Large hematomas mimic intraperitoneal emergencies, such as adnexal torsion or placenta percreta, bleeding into the extrauterine compartment (Fig. 26.14). For a more accurate diagnosis, US findings can be compared with US



**Fig. 26.13** Longitudinal sonogram shows a heterogeneous hypoechoic mass (*calipers*) at the deep aspect of the abdominal wall. (Reproduced with permission from [161])



**Fig. 26.14** (a) Abdominal sonography shows a heterogeneous hypoechoic mass (*arrowhead*) adjoining the placenta (*arrow*). (b) Doppler sonography shows vascularity with

blood flowing around the mass (*arrowhead*) and between the mass and the placenta (*arrow*). (Reproduced with permission from [187] under the CC Attribution License)

findings made earlier in the same pregnancy [161]. In uncertain cases, Doppler US shows a nonvascularized structure (Fig. 26.14).

#### 26.4.7.2 Abdominal CT

CT appearances can distinguish three types of RSH in the general population. *Type I* is unilateral and contained within the muscle; *type II* is uni- or bilateral and has blood between the muscle and transversalis fascia (Fig. 26.15); *type III* invades the prevesical space or peritoneum and

may or may not affect the muscle [173]. This classification can be used in pregnancy for the treatment strategy.

With the improved accuracy of the US, the CT and technetium-99-labeled red blood cell scintigraphy use are limited [161].

#### 26.4.7.3 Abdominal MRI

Abdominal MRI accurately shows RSH dimensions which help in the decision on the type of treatment (Fig. 26.16).

#### 26.4.7.4 Angiography

The IEA represents a potentially overlooked source of pelvic arterial hemorrhage. The IEA should be considered a possible source of arterial hemorrhage if the arteriography of internal iliac artery branches does not yield a bleeding source [169].

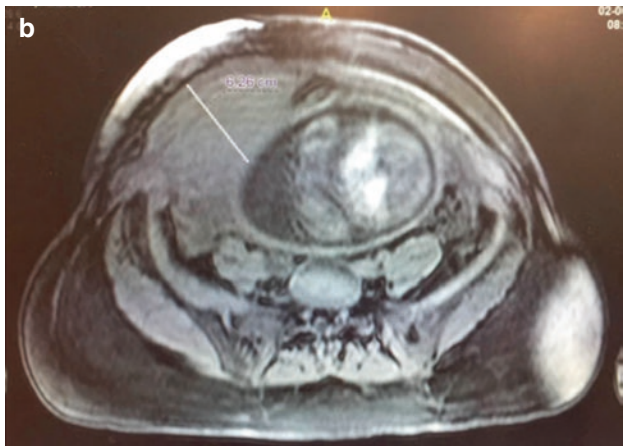
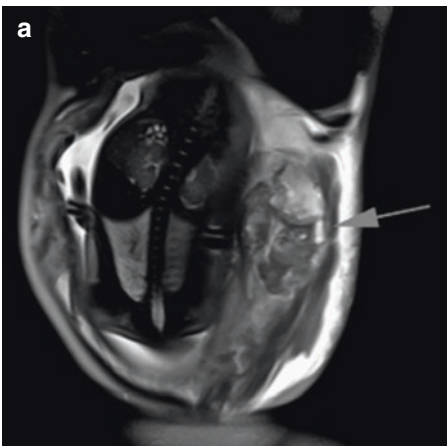
### 26.4.8 Treatment

#### 26.4.8.1 Conservative Treatment

Hemodynamic stability and the hematoma type determine spontaneous RSH management. RSH Type I usually spontaneously resolves uneventfully within 1–2 weeks, although the complete resolution of the hematoma may take as long as



**Fig. 26.15** A left-sided rectus sheath hematoma type II ( $14.0 \times 12.7 \times 10.1$  cm) extending to the left thoracic wall at 25 weeks of pregnancy. (Reproduced with permission from [161])



**Fig. 26.16** (a) Abdominal MRI (coronal T2-weighted) shows a large left-sided rectus sheath hematoma  $160 \times 70 \times 55$  mm (arrow). Note the subcutaneous fat stranding and a small hemoperitoneum coexisting with a fetus of 33

weeks. (Reproduced with permission from [165]). (b) Abdominopelvic MRI shows  $26 \times 6.3 \times 7.7$  cm rectus sheath hematoma anterior to the gravid uterus at 28 weeks gestation. (Reproduced with permission from [183])

2–3 months. Treatment consists of rest, peroral analgesia, cold compresses on the skin over hematoma, and temporary discontinuation of anticoagulation in consultation with the specialist prescribing anticoagulation. After resolution, RSHs usually do not recur and typically do not cause long-term sequels. RSH Type II is treated as RSH Type I with the addition of packed red blood cells. Only 30% are treated conservatively due to incorrect preoperative diagnosis [183].

Most patients are treated with peroral NSAIDs or opioids for pain relief. Transversus abdominis plane block eliminates a large dosage of peroral analgesia [170].

#### 26.4.8.2 Transarterial Embolization

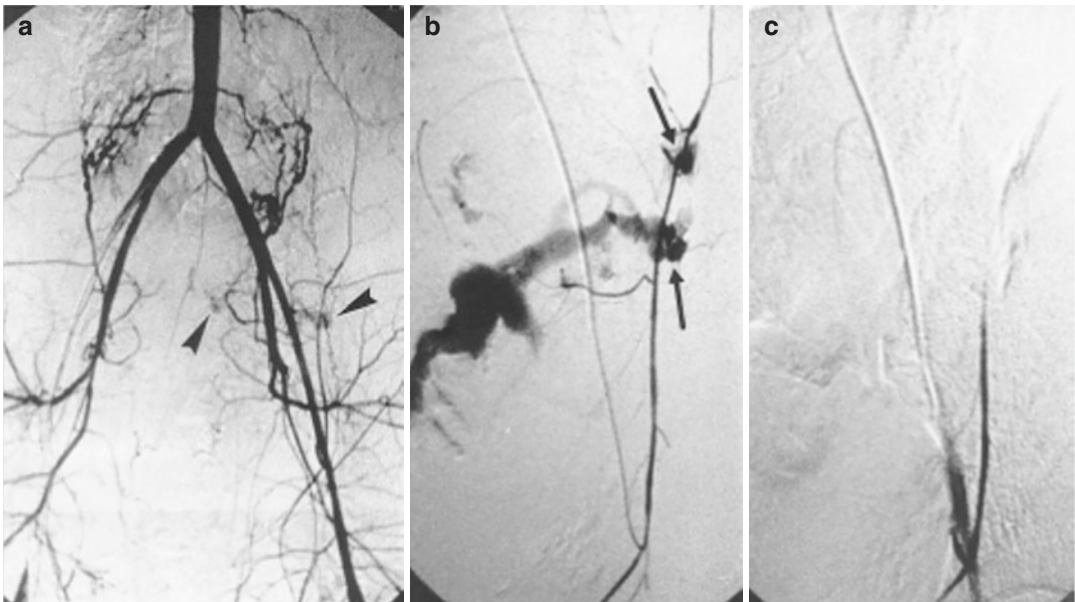
Almost all cases of bleeding IEA after CS are treated by transarterial embolization (Fig. 26.17) [168, 169, 188], rarely conservatively [170].

Identifying a bleeding point helps guide management. A massive hematoma extending into the retroperitoneum may originate from a bleeding IEA or a retroperitoneal structure such as a leaking iliac or abdominal aortic aneurysm. Selective percutaneous transcatheter arterial

embolization is an effective hemostatic for large RSH [165]. Regarding the safety of embolization during pregnancy, the general late-onset of this pathology reduces the risks associated with fetal irradiation. The large RSH displaces the uterus and the fetus to the contralateral side, reducing the dose of X-rays delivered to the fetus [165]. Selective epigastric embolization in severe RSH during the third trimester of pregnancy should be considered the potential primary and alternative management path to laparotomy. However, this technique is time-consuming, expensive, and not always available. This procedure is also associated with contrast-induced nephropathy or bleeding from the puncture site. Another disadvantage is that the bleeding vessel cannot always be identified. Further studies are required to confirm that the maternal and fetal benefits outweigh the fetal risks associated with embolization.

#### 26.4.8.3 Surgical Treatment

Intraperitoneal rupture, infection, or active bleeding with unstable hemodynamics mandates prompt surgical intervention. If the hematoma is very extensive and when the shock is controlled,



**Fig. 26.17** (a) Aortiliac arteriogram shows abnormal stains (arrowheads) on the left side of the pelvis. (b) Selective left inferior epigastric arteriogram showing

massive bleeding from two injured portions (arrows). (c) Complete occlusion of bleeding points after embolization. (Reproduced with permission from [168])

a paramedian incision with a section of the rectus sheath and retraction of the muscle laterally will facilitate visualization of the bleeding vessel. The suture of the ruptured vessel or muscle should be performed. Intraperitoneal rupture is treated by laparotomy, evacuating blood and clots and controlling bleeding. With hemodynamic stability, laparoscopy is diagnostic and therapeutic with bleeding control depending on its cause.

Complication as an infection of RSH has two forms: infected hematoma or necrotizing infection as the complication of post-CS RSH (with additional external trauma) [182]. Evacuation of infected hematoma is mandatory with bacterial swabs and drains in the abscess cavity.

#### 26.4.8.4 Obstetric Management

In more than 50%, emergent CS is performed because the preoperative diagnosis was incorrect in 60% [161, 183] and pointed to the urgent condition that mandates CS. It seems safe to allow patients with a history of RSHs to deliver vaginally regardless of initial RSH treatment. There were no reported recurrences of RSHs after operative or expectant treatment [161].

### 26.4.9 Prognosis

#### 26.4.9.1 Spontaneous Rectus Sheath Hematoma

While frequently self-limiting, RSH in the general population can result in severe complications and carry a mortality risk of 4% [189].

Until 1929, maternal and fetal mortality during pregnancy were 0% and 37.5%, respectively, while during labor, maternal and fetal mortality were 0% [163]. Until 1943, maternal and fetal mortality were 15% and 50%, respectively [164]. Reports from the 1950s claim maternal and fetal mortality of 12% and 25%, respectively. Until 1997, maternal and fetal mortality were 11% and 34%, respectively [176]. RSH can contain up to 2 L of clot and blood. This amount leads to fetal hypoperfusion with the additional impact of abdominal compartment syndrome [185].

A 60% of incorrect initial diagnoses [161, 183] are associated with an increased rate of

exploratory laparotomy, CS, prematurity, and perinatal death. A misdiagnosis of RSH as placental abruption may lead to early delivery rather than expectant management [161].

## 26.5 Omental Infarction

### 26.5.1 Incidence

Pietro de Marchetti described the first case of omental torsion in the general population in 1858. Up to 1986, a few hundred cases have been published in English literature [190], while up to 2012, approximately 400 have been reported [191]. About 85% have occurred in adults, most frequently in the age group of 40–50 years and male:female ratio of 2:1 [191].

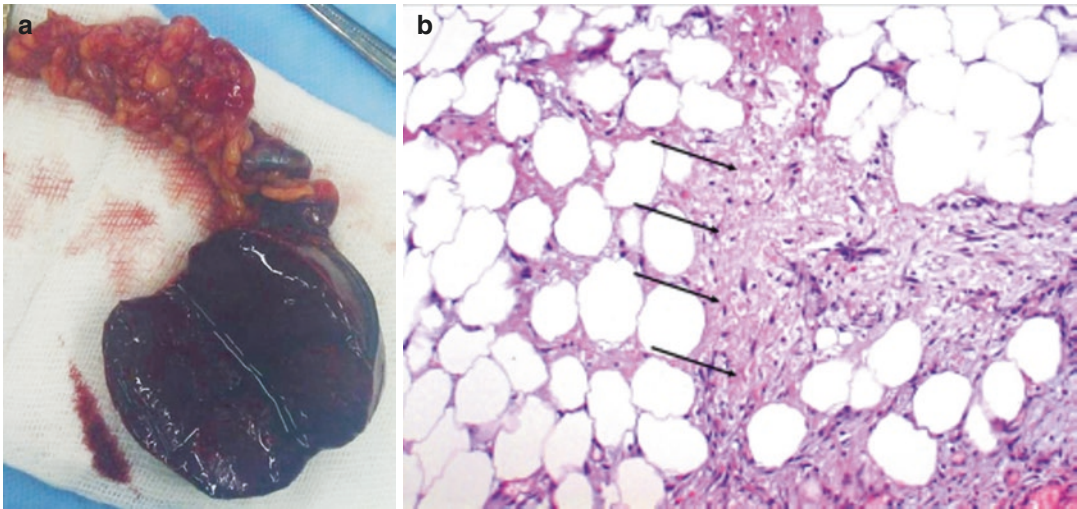
JL Bubis (Chief, Department of Gynecology and Obstetrics, Mt. Sinai Hospital, Cleveland, Ohio, USA) reported the first omental torsion during pregnancy [192]. Omental torsion presents in the second half of pregnancy [192–197], with two “early” cases in the 17th and 19th gestational weeks [198, 199]. It presents in the early puerperium after CS [200, 201] or vaginal delivery [202, 203].

### 26.5.2 Etiology

Torsion of the omentum in the general population is the leading cause of infarction. In 1948, Anton et al. classified omental infarction into primary and secondary types [204]. Primary torsions are defined when no other intra-abdominal pathology is found, while secondary torsions include tumors, cysts, inflammatory changes, adhesions, or abdominal wall hernias. Predisposing factors for torsion are anomalies of the omentum, such as a small root, irregular vascular anatomy, abdominal trauma, cough, and physical strain [205]. Depending on the duration and the degree of torsion, omental necrosis ensues (Fig. 26.18).

The etiology of omental infarction without torsion remains uncertain. Several mechanisms have been proposed, such as an anomaly of the





**Fig. 26.18** (a) Torsion of a right lower segment of omentum resulting in omental gangrene. (Reproduced with permission from [193] under the CC BY 3.0). (b) Histological findings of major omentum show fresh hemorrhagic cir-

culations disorders (arrows), partial necrosis of fatty tissue with acute inflammatory cell infiltrate (hematoxylin, 100 $\times$ ). (Reproduced with permission from [202] under the CC BY 2.0)

venous vessels [206]. Other causes of primary infarctions are hemostasis or vascular diseases exaggerated during pregnancy and the puerperium when hypercoagulability leads to thromboembolic events [207].

The exact mechanism leading to infarction in puerperium remains unclear. A possible increase in intra-abdominal pressure during labor, a high decrease in uterine volume immediately after the labor, and the return of the mother's body to the prepregnancy physiological condition may have provoked the torsion.

Patients with normal vital signs are not in acute distress [195]. The O<sub>2</sub> saturation is normal [194]. Physical examination of the abdomen reveals localized peritoneal irritation on the right side or epigastrium when infarction is present. Omental torsion without infarction presents only with tenderness [194]. The patient is primarily afebrile [193–195, 202] or rarely with low-grade fever when omental necrosis or abscess develops. Bowel sounds are normal [194, 195].

The obstetric examination is normal [194].

### 26.5.3 Clinical Presentation

In the early phase, patients complain of epigastric or right upper quadrant abdominal pain that can last from hours to days [194, 195]. Symptoms include a constant “gnawing” pain with occasional radiation to the left upper quadrant. The pain is alleviated by standing and exacerbated by sitting and lying supine [194]. These symptoms could be recurrent or intermittent during pregnancy [192, 194]. Nausea and vomiting are primarily absent [193, 195].

### 26.5.4 Differential Diagnosis

The clinical presentation often misleads to incorrect preoperative diagnosis (Table 26.3).

### 26.5.5 Diagnosis

#### 26.5.5.1 Laboratory Findings

The C-reactive protein and white blood count may be elevated [194, 195, 202] depending on whether the (partial) necrosis of the omentum



**Table 26.3** Differential diagnosis of omental torsion during pregnancy [193–195, 200, 202]

|                               |
|-------------------------------|
| Acute cholecystitis           |
| Acute appendicitis            |
| Colonic diverticulitis        |
| Appendagitis epiploica        |
| Incarcerated umbilical hernia |
| Adnexal torsion               |
| Myocardial infarction         |

occurred. Other serum markers and urinalysis are normal [194, 202].

### 26.5.5.2 X-Rays

Plain abdominal and chest radiographs are usually normal [194].

### 26.5.5.3 Transabdominal Ultrasound

The transabdominal US is often unremarkable. Sometimes minimal free fluid is noticed [195]. A common differential diagnosis is acute cholecystitis, and the US shows normal gallbladder [194]. The transabdominal US confirms fetal status [193].

### 26.5.5.4 Abdominal CT

As most patients show symptoms of an acute abdomen, CT of the abdomen and pelvis should be the diagnostic imaging of choice in the general population [208]. If omental infarction is caused by torsion, characteristic CT findings might be detectable. The torsion leads to concentric linear strands in the fatty mass, a so-called *fat spiral pattern* (Fig. 26.19).

Differentiating the omental infarction from other abdominal or omental diseases is challenging, and the radiological findings could be misinterpreted as an incarcerated umbilical hernia [202].

### 26.5.5.5 Diagnostic Exploration

Diagnosis of an omental infarction has traditionally been made intraoperatively at an exploratory laparotomy or laparoscopy. If there is another pathology, it should be treated during the exploration. Diagnostic exploration is difficult in the third trimester when omental infarction is most common.



**Fig. 26.19** Abdominal CT shows a hypoperfused mass in the anterior portion of the median epigastrium with fatty density (white arrows) and a thin layer of free fluid surrounding the liver. (Reproduced with permission from [202] under the CC BY 2.0)

### 26.5.6 Treatment

#### 26.5.6.1 Conservative Treatment

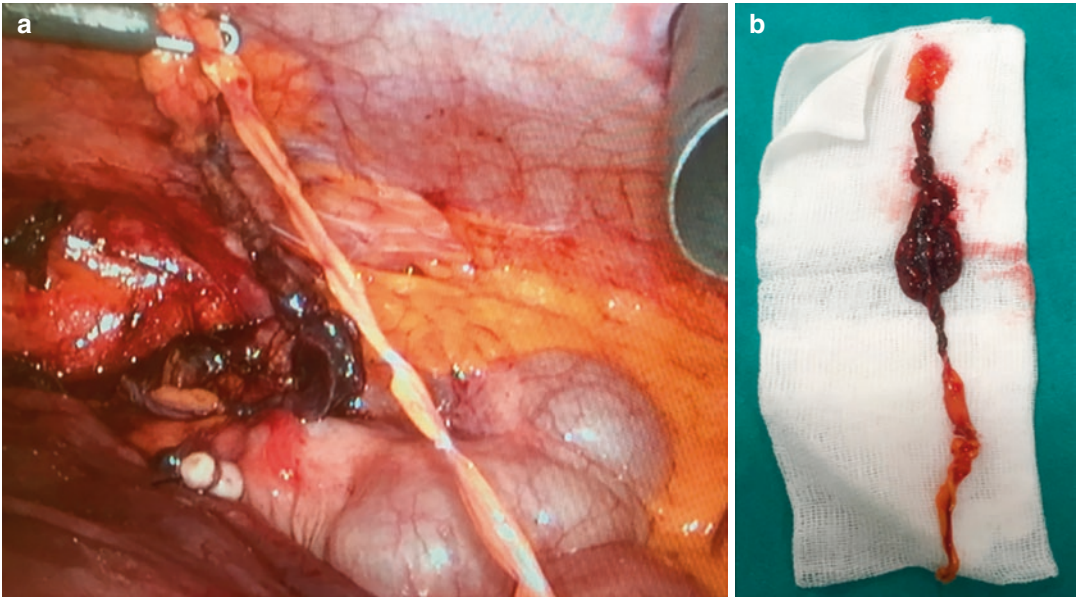
In the general population, when the diagnosis is made by imaging, conservative treatment is preferred because the disease is self-limited [191]. Emergent surgical intervention is indicated whenever conservative treatment fails or the patient's clinical status worsens.

#### 26.5.6.2 Surgical Treatment

Surgical exploration leads to the diagnosis without an accurate preoperative diagnosis (Fig. 26.20). Macroscopically changed greater omentum should be resected (total or partial omentectomy) to eliminate recurrent torsion or secondary infection from omental necrosis. In only one case with a preoperative diagnosis of acute appendicitis, appendectomy was done simultaneously with partial omentectomy [199].

### 26.5.7 Prognosis

The prognosis is excellent. The disease rarely influences the fetal outcome. Pregnancies are completed with uncomplicated term deliveries of healthy newborns [192–195, 198, 199] or with CS near-term during exploration [196, 197]. The maternal outcome is also excellent due to the benign nature of the primary disease [195–200, 202].



**Fig. 26.20** (a) Laparoscopic view of twisted omentum with necrosis. (b) Excised segment of omentum. (Reproduced with permission from [195] under the CC Attribution License)

## 26.6 Gastrointestinal-Genital Communications

### 26.6.1 Introduction

In some cases, it is more precise to define the pathologic process as communication or infiltration than fistula due to the close contact between gastrointestinal and genital organs that produce symptoms without a true channel between them.

### 26.6.2 Incidence

Communication of the gastrointestinal tract with the genital system from any cause is unusual. Until 1933, with the previous 200 years included, 58 cases were collected in the general female population [209]. Until 1956, 80 cases of enterouterine fistula were collected—52.5% followed an obstetric injury [210].

In over 1,000 consecutive cases of ectopic pregnancy at the Cook County Hospital (1940–1956), only one was associated with bowel inva-

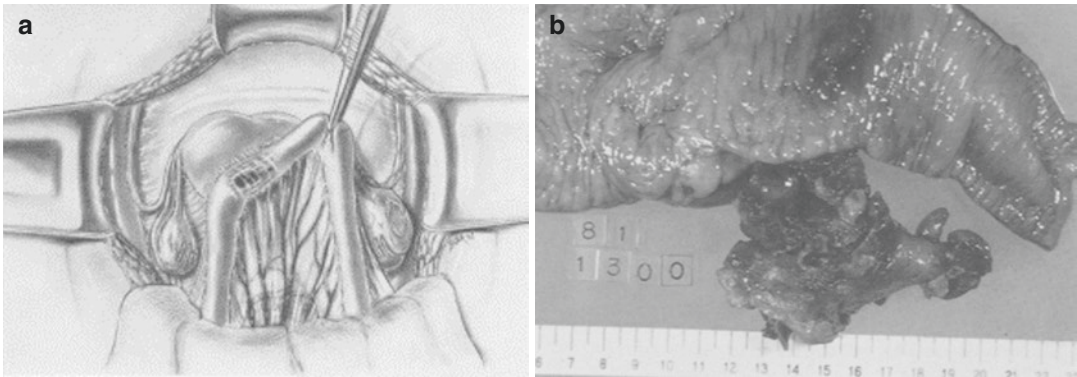
sion [211]. Enteroamniotic fistulas from ectopic pregnancy are even more unusual, with 26 cases published [211–235]. The first known case is by Armstrong, in 1835, of a woman in her sixth month of pregnancy who suddenly passed bloody stools containing fetal bones and died from bleeding [212].

### 26.6.3 Etiopathogenesis

#### 26.6.3.1 Enterouterine Fistula

Le Jemtel, in 1909 [236], presented an etiological classification of enterouterine fistulas updated by Hawkes [237]. Four major etiological categories include:

- Malignant—by infiltration and invasion arising in either the bowel or uterus,
- Peritonitis—from trauma, puerperal infections, intestinal inflammation, and fistulas following abscess formation involving the inflamed adjacent walls of both the uterus and intestine,



**Fig. 26.21** (a) Terminal ileum firmly attached to the left cornu of the uterus with a fistula between ectopic gestation and small bowel wall with lumen exposed. (Reproduced with permission from [214]). (b) Terminal

ileum with a perforated lesion of  $5 \times 4$  cm and the Fallopian tube pregnancy constituted by blood clots with small areas of yellowish villous material. (Reproduced with permission from [221])

- Traumatic or spontaneous rupture of the gravid uterus with strangulation of a loop of bowel caught in the defect,
- Instrumental transvaginal uterine perforation.

The most common cause is complicated Crohn's disease [238–241]. A small nongravid uterus is deep in the pelvis, posterior to the bladder, without contact with the terminal ileum. This is likely responsible for the rarity of enterouterine fistulas. Pregnancy increases the risk as the enlarging uterus spreads out of the pelvis and into proximity to the terminal ileum. Most cases of enterouterine fistula occurred in puerperium [238–241].

Unsafe abortion is still common in undeveloped countries. It can result in enterouterine fistula [242], intestinal obstruction (see Sect. 18.3), or intestinal perforation (see Sect. 22.4.2.5).

### 26.6.3.2 EnteroAmniotic Fistula

#### Extrauterine/Abdominal Pregnancy

Francis E. Stock, in 1944, described the role of infection in secondary abdominal pregnancy complicated by fistula and rupture through the umbilicus [243]. The approximation of a vascular placenta, with the potential of villous invasion of adjacent structures, to the intestine, creates a precarious set of circumstances. Following the vil-

lous invasion of the bowel wall, on the approximation of the gestational sac to the intestine, inflammatory reaction and infection may create fistula formation. The source of infection may vary according to the location of the ectopic sac. Intraperitoneal ectopic sacs are most commonly infected from the adjacent bowel, whereas intraligamentary sacs are often contaminated by bacteria from the vagina or uterus [243]. The gestational vascular structures aggravated by infection and villous invasion of adjacent vascular structures provide a dangerous source of massive bleeding (Fig. 26.21).

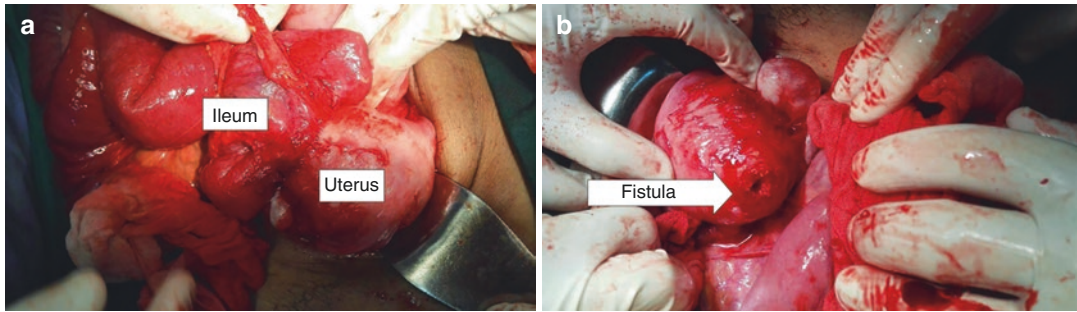
Similarly, following the villous invasion of the bowel wall, chorioamnionitis results from a fistula between the gestational sac and the bowel [214].

#### Obstetric Cause

The two most common causes of enterouterine fistula are CS (Fig. 26.22) and endoluminal uterine instrumentation, most commonly transvaginal instrumental abortion or curettage [245].

### 26.6.4 Prevention

The importance of meticulous surgical technique in reoperation of the pelvic floor, uterus, and Fallopian tubes and the manipulation of the



**Fig. 26.22** (a) Small bowel adherent to the posterior wall of the uterus. (b) The ileouterine fistula observed after separation of the bowel loops. (Reproduced with permission from [244] under the CC BY 3.0)

bowel was stressed by Engel [215]. Postmortem examination illustrated how inadequate reperitonealization of the uterus during a previous ipsilateral salpingo-oophorectomy allowed a loop of the ileum to become adherent to the uterus. This set of circumstances made perforation of the adjacent ileum by a subsequent interstitial pregnancy more likely, ultimately costing the patient her life due to profuse bleeding into the bowel from an intrauterine vessel.

### 26.6.5 Clinical Presentation

The clinical presentation is different depending on the advancement of pregnancy, location, type, genital, and end gastrointestinal organ. Hours to days after the instrumental abortion, the patient with enterouterine fistula commonly presents with passing the semiformal fecal matter through the vagina. This could be the only symptom without signs of peritonitis or partial/complete bowel obstruction [242].

Expulsion of fetal parts or disintegrated fetal bones per rectum indicates a fistulous tract between the genital tract or extrauterine pregnancy and the gastrointestinal tract [246].

Rectal bleeding can be the only sign in the rectosigmoid location of infiltration or perforation [223]. Depending on the severity and duration of the bleeding, the patient can present in severe hemorrhagic shock or just pallor as a sign of bleeding [216]. Ectopic pregnancy infiltrating the intestine should be suspected with simultaneous

or sequential vaginal and rectal bleeding [216]. The most common sequence of symptoms of ectopic pregnancy resulting in rectal bleeding is [211–235]:

- Amenorrhea,
- Lower abdominal pain,
- Vaginal bleeding,
- Rectal bleeding.

Vaginal bleeding can precede abdominal pain [221]. Instead of rectal bleeding, the patient can present with melena; fetal parts could protrude through the anus [247] or bowel wall during the proctoscopy or colonoscopy.

### 26.6.6 Diagnosis

#### 26.6.6.1 Endoscopy

If the bleeding is in the rectum, the proctoscopic examination can reveal bleeding or a defect in the anterior wall of the rectal mucosa, sometimes with active bleeding [223]. If proctoscopy examination does not reveal the bleeding site or the blood comes from the upper portions of the colon, sigmoidoscopy [216] or colonoscopy should be performed.

#### 26.6.6.2 Hysterosalpingography

Hysterosalpingography can reveal communication with the gastrointestinal tract. The contrast put through the cervix into the uterine cavity is seen in the bowel loops (Fig. 26.23).





**Fig. 26.23** Absence of opacification of the uterine cavity and beginning of opacification of the bowel loops. (Reproduced with permission from [245])

## 26.6.7 Treatment

Unlike in the general female population, gastrointestinal-genital communications (fistulas) represent true emergencies due to deleterious consequences to the fetus itself and the normal progression of pregnancy.

Early laparotomy and minimal surgery on the involved bowel improve maternal survival.

### 26.6.7.1 Gastrointestinal-Genital Fistula

Knowledge of the possibility of fistula formation between an ectopic gestational sac and bowel and suspicion of its presence is essential for successful management. Intestinal hemorrhage in any potentially pregnant woman should stimulate

consideration of this dangerous condition. Considering the role of an inevitable presence of infection necessitates complete excision of all involved structures when possible [234]. When technically feasible, all structures, including the uterus, should be excised when involved in the infected fistula and inflammatory process (Fig. 26.24).

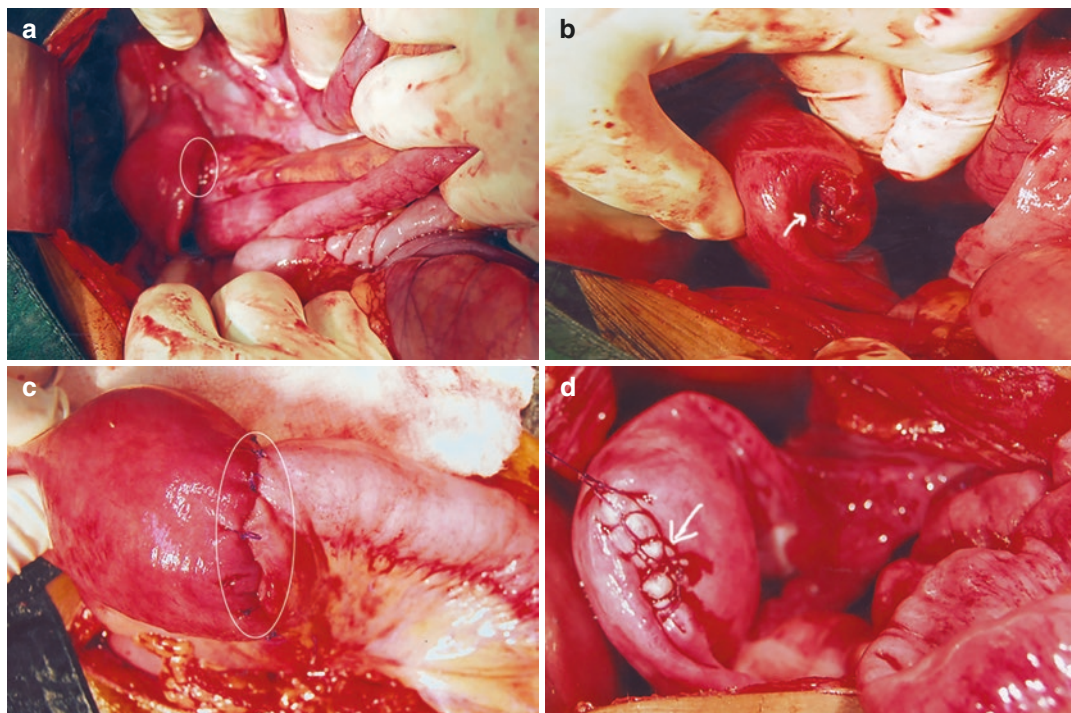
### 26.6.7.2 Abdominal Pregnancy

An exception from the previous rule of complete excision is abdominal pregnancy, where the extensive intimate invasion of the surrounding structures by the placenta makes removal dangerous and usually impossible. Surgery in abdominal pregnancy with bowel invasion is more hazardous than in uncomplicated abdominal pregnancy, where the placenta can be left undisturbed even though the vascular supply of major organs is involved (see Sect. 9.3.7.2). Even in this situation, consideration should be given to the resection of as much involved tissue as possible with drainage to prevent intra-abdominal abscess formation. In simple fistula formation with only a small opening into the intestine and the absence of marked inflammatory reaction, simple closure of the bowel is acceptable. Otherwise, in the emergent setting, segmental resection with end-to-end anastomosis in the case of the small bowel and right colon or diverting colostomy with the involvement of the left colon and rectum is indicated.

## 26.6.8 Prognosis

Until 1961, the mortality of ectopic pregnancy causing rectal bleeding or melena was near 100% from the hemorrhagic shock. This resulted from the delay in diagnosis and treatment and complications after resection of the involved segment of the bowel [211–213, 215]. After 1961, maternal survival is more than 90%. It is even higher in developed countries because a higher mortality rate in undeveloped countries leads to a lower rate of these complications.





**Fig. 26.24** (a) Ileal loop adherent to the fundus of uterus posteriorly; (b) perforation of uterine fundus posteriorly near left cornu; (c) resection with ileal end-to-end anasto-

mosis (Note the dilated proximal ileal loop); (d) closure of uterine perforation in two layers. (Reproduced with permission from [242])

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## Part IV

## Urology

## Complicated Urinary Tract Infections

# 27

### Abstract

Urinary tract infections (UTI) are more common during pregnancy. Asymptomatic bacteriuria is present in 2–15% of pregnant women, while symptomatic UTI, cystitis, and acute pyelonephritis complicate 1–2.5% of pregnancies. In pregnancy, urinary stasis and vesico-ureteral reflux are caused by hormonal and mechanical changes. The enlarging uterus can obstruct the ureters and compound urinary stasis, explaining why complicated pyelonephri-

tis was seen more in the latter half of pregnancy. Urinalysis, urine culture, and transabdominal ultrasound are usually diagnostic. Procalcitonin is highly sensitive and specific along with the clinical presentation. Treatment is mostly conservative, based on antibiotics. Acute pyelonephritis in pregnancy leads to a higher likelihood of preterm delivery. Urosepsis may be related to an increased cerebral palsy rate among preterm infants. Preterm delivery results in a higher low birth-weight rate.



## 27.1 Anatomic and Functional Changes of the Urinary Tract During Pregnancy

### 27.1.1 Upper Urinary Tract

Morgagni described upper urinary tract dilatation in pregnancy in 1761 and Rayer in 1839 discerned from postmortem examination, and then Erich Carl Otto Opitz described it in 1905 (Fig. 27.1) [2]. They stated that the gravid uterus compresses the ureters and causes dilatation of structures such as the ureters, pelvis, and calyces. Also, increasing progesterone causes relaxation in the smooth muscles of the urinary system. The result is delayed urine excretion and urine retention in the kidneys [3]. The kidneys elongate 1–1.5 cm in a normal pregnancy due to increased vascular volume, interstitial space/fluid [4], and

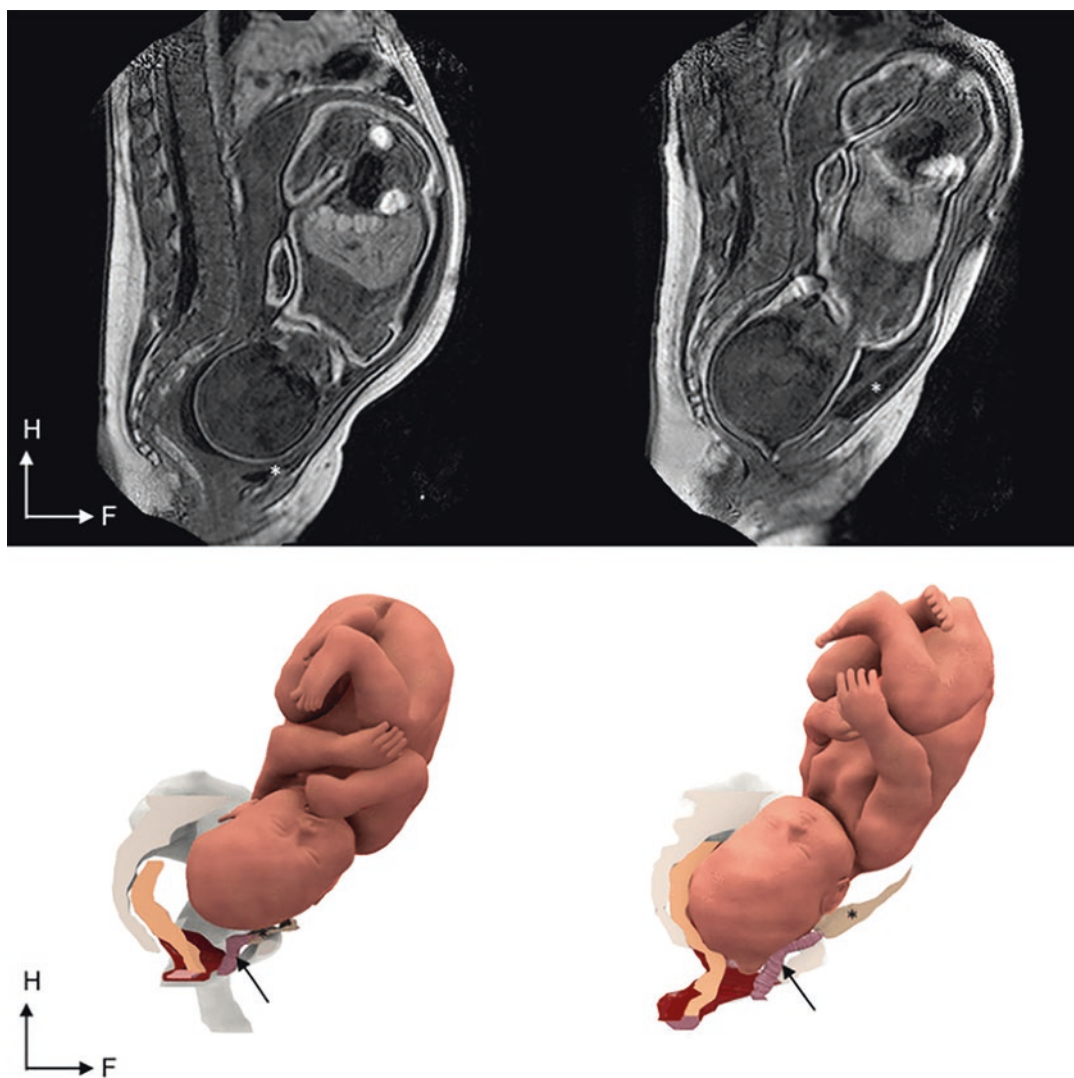
glomerular filtration rate by 50% [5]. With the increase in the pelvic vasculature in pregnancy, the right ureter is affected more often (80%) [3] than the left because it crosses a less rigid right iliac artery proximal to the pelvic brim and the right ovarian blood vessels [6]. Stadfeldt reported right hydroureteronephrosis caused by uterine compression of the ureter at the level of the iliac vessels in 1861 [7]. Abnormal ureteral peristalsis has not been consistently found [8]. Approximately 90% have detectable asymptomatic hydronephrosis [9], while only a minority progresses to anuria, urinary tract rupture, or renal failure. The dilatation involves only the renal, pelvic, and abdominal ureter. This effect usually resolves in 50% within 2 days of delivery.

### 27.1.2 Lower Urinary Tract

During pregnancy, especially in advanced pregnancy, the urinary bladder is compressed at its dome (Fig. 27.2). Intravesical pressure increases from 9 to 20 mmH<sub>2</sub>O, corresponding to a urethral closure pressure increase [11]. Cystoscopically, an indentation of the bladder dome by the enlarged uterus, is visible during pregnancy, and the ureteric orifices are in a higher position than in the nonpregnant state [12]. During fluoroscopy, alterations in the bladder profile are present (Fig. 27.3). Vaginal delivery predisposes to prolapsed pelvic organs [14], including loss of support for the anterior vaginal wall and bladder. Also, vaginal delivery and pregnancy are associated with increased mobility and descent of the bladder and other pelvic organs. At term, the bladder neck descends with Valsalva approximately 5 mm more in pregnant women than in nonpregnant controls [15], and almost half of primiparous women have pelvic organ prolapse stage 2 (the leading edge of the vaginal walls or cervix comes to at least within 1 cm of the hymen) [16,

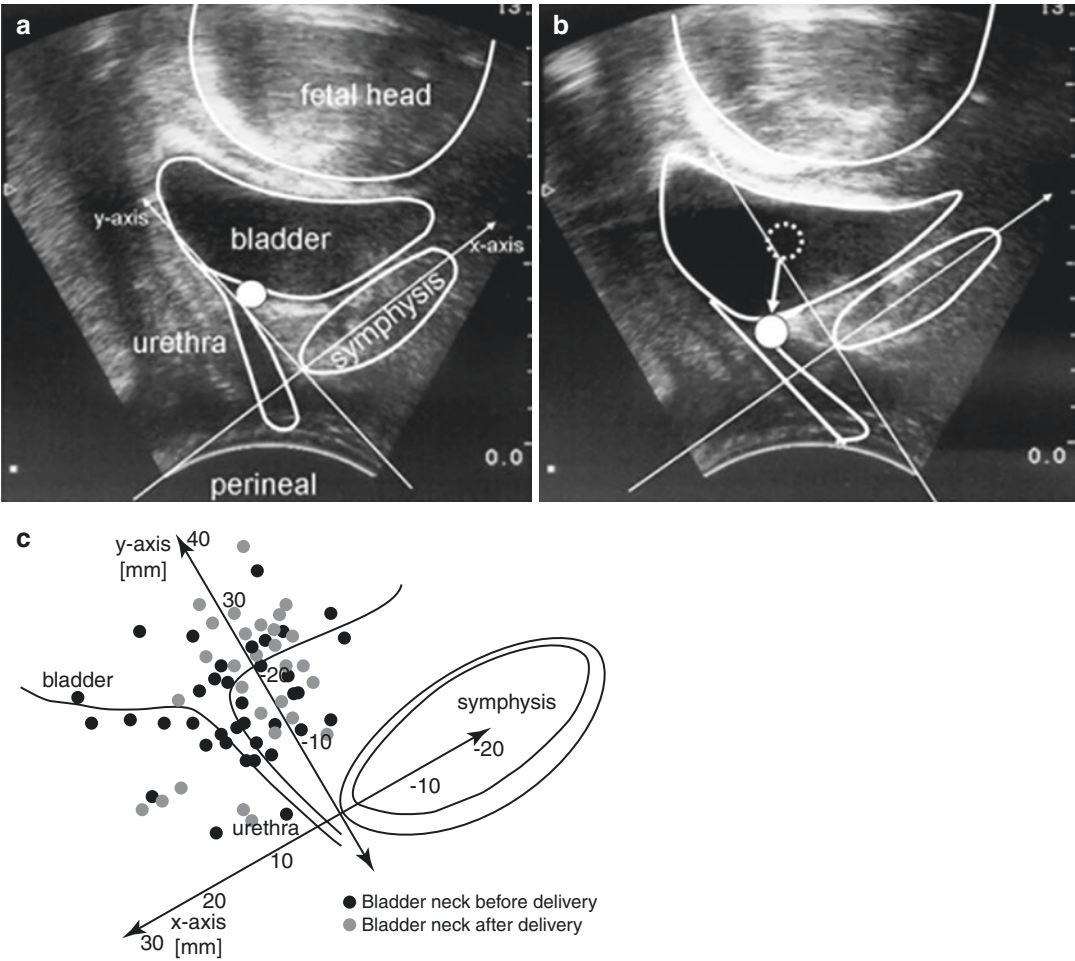


**Fig. 27.1** Erich Carl Otto Opitz (1871, Breslau–1926, Garmisch), a German gynecologist and the editor of the journal *Deutsche Frauenheilkunde*. (Reproduced with permission from [1])



**Fig. 27.2** Imaging of the bladder before (left) and during (right) the second phase of labor in MRI slices (up) and 3D (down). Before labor, the bladder is located between the fetal head and the pubis. The fetal head's descent causes the bladder, in semi-repletion at that point, to move

upward into a suprapubic position. Simultaneously the urethra is lifted (*arrow*) and pushed against the internal surface of the pubis. (Reproduced with permission from [10])



**Fig. 27.3** Bladder neck (a) at rest and (b) with Valsalva maneuver. A point indicates the bladder neck. An arrow is a vector for bladder neck mobility. (c) Position of the

bladder neck before and after delivery at rest. (Reproduced with permission from [13])

[17]. The descent of the anterior vaginal wall and bladder to the level of the hymen by the third trimester of pregnancy is normal, usually asymptomatic, and usually resolves after delivery. In this setting, the presence of anterior vaginal wall descent or “cystocele” does not merit investigation or treatment.

**27.1.3 Composition of the Urine**

Urolithiasis results from the anatomical and physiological changes in the urinary system during pregnancy, including changes in the chemical properties of urine (Table 27.1).

**Table 27.1** Physiologic changes related to urolithiasis during pregnancy

| Stone-inducing factors                                                                                                                          | Stone inhibitors factors                                                                                                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|
| Increased renal blood flow, leading to a 30–50% rise in glomerular filtration rate                                                              | Increased excretion of citrate, magnesium, glycoproteins, uromodulin, and nephrocalcin (increased glomerular filtration rate) |
| Increased filtered loads of calcium, sodium, and uric acid                                                                                      |                                                                                                                               |
| Hypercalciuria is enhanced by placental production of 1,25(OH)2D3, which increases intestinal calcium absorption and secondarily suppresses PTH |                                                                                                                               |
| Hyperuricosuria as a result of an increased filtered load of uric acid                                                                          |                                                                                                                               |

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## 27.2 Symptomatic Urinary Tract Stones

### 27.2.1 Incidence

Urinary stone disease affects 10% of the population in a lifetime. This rate is attributed to increased imaging, changes in dietary habits and climate conditions, and rising obesity and diabetes mellitus [19–22]. Although urinary stone disease used to be more widespread amongst men, the difference between genders disappeared with increased urinary system stone incidence in women [22, 23]. Urinary stone disease is observed in 1/200 to 1/2000 pregnancies [24, 25], on average in 0.5% of pregnant women [26]. No difference exists in prevalence between pregnant and nonpregnant groups of similar age [27, 28].

### 27.2.2 Etiopathogenesis

Urolithiasis/nephrolithiasis is related to dietary habits, climate conditions, obesity, and diabetes mellitus [19–22]. Anatomical and physiological changes during pregnancy influence the chemical properties of urine (see Sect. 27.1.3). Increasing glomerular filtration, calcium supplement treatments, and vitamin D levels increase calcium excretion in the urine [29–31]. Furthermore, uric acid, sodium, oxalate, and other lithogenic factors increase during pregnancy [30, 31]. Calcium phosphate stones are observed in 75% of pregnant women, whereas in the general population, calcium oxalate stones are usually present [28, 32, 33].

### 27.2.3 Clinical Presentation

The most common signs/symptoms are flank pain (89%) and microscopic hematuria (95%) [24]. In asymptomatic patients, colicky pain and hematuria may be absent due to the physiological dilatation of the ureter. Urinary tract infection (UTI) can present with fever and chills. Acute renal colic in the later stages of pregnancy could

be due to a sudden shift in uterine position reinforced by the natural tonus of the abdominal musculature. The colic is relieved by the postural change to the left lateral position when the right kidney is involved or assuming the knee-chest position [34, 35]. This suggests that the colic originated from external compression by an enlarged uterus.

### 27.2.4 Differential Diagnosis

Differential diagnosis of symptomatic upper urinary tract stones includes pyelonephritis in pregnancy (see Sect. 27.3.4). With acute and severe pain, differential diagnoses include ruptured renal artery aneurysm (see Sect. 29.2), renal collecting system rupture (see Sect. 28.2), renal vein thrombosis, and renal infarction.

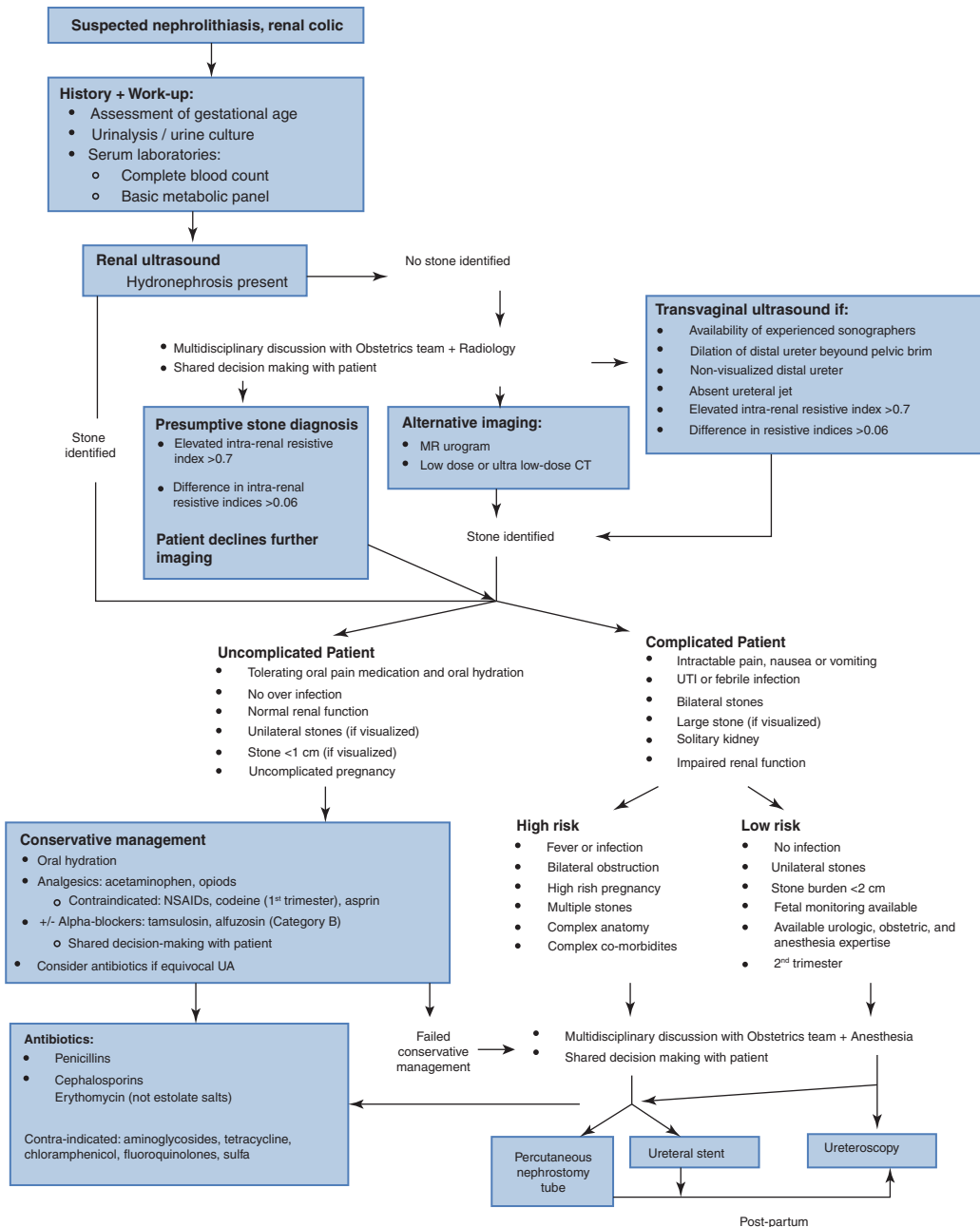
### 27.2.5 Diagnosis

The rate of negative ureteroscopy in pregnant women is 14% [36]. Since the physiologic dilation can be misdiagnosed as obstruction by a stone of the distal part of the ureter, the role of imaging methods becomes prominent. This avoids invasive procedures based on false-positive results eliminating procedure-related complications. The diagnostic algorithm is presented in Fig. 27.4.

#### 27.2.5.1 Laboratory Findings

In pregnancy, recommendations for the evaluation of the nonpregnant population by the *American Urological Association* are [38]:

- Serum intact parathyroid hormone level should be obtained as part of the screening evaluation when primary hyperparathyroidism is suspected,
- When a stone is available, a stone analysis should be obtained at least once,
- Additional metabolic testing is recommended in high-risk or interested first-time stone formers and recurrent stone formers,



**Fig. 27.4** Diagnostic-therapeutic algorithm for pregnant patients with suspected urolithiasis [37]

- Metabolic testing should consist of one or two 24 h urine collections obtained on a random diet and analyzed at a minimum for total volume, pH, calcium, oxalate, uric acid, citrate, sodium, potassium, and creatinine.

### 27.2.5.2 Abdominal Ultrasound

#### Transabdominal Ultrasound

Despite 60–78% sensitivity, the first diagnostic tool in pregnancy is grayscale ultrasound (US)



[39, 40]. Ureteral stones might be difficult to demonstrate with the US. Therefore, assessing the resistive index (RI) ( $>0.70$ ) with Doppler increases the sensitivity up to 90% to display the obstruction (although without stone detection) [41, 42]. Although RI cannot reveal the cause of obstruction, it is crucial to show the necessity of intervention. Also, the US has low accuracy for defining complications of obstruction, such as renal collecting system rupture (see Sect. 28.2).

### Transvaginal Ultrasound

The transvaginal ultrasound (US) distinguishes physiological hydronephrosis, observed in 90% of pregnant women, from ureteral stones in the distal ureter [29, 43].

#### 27.2.5.3 Abdominal CT

In the nonpregnant state, an unenhanced computed tomography (CT) is a gold standard for diagnosing urinary stones [44, 45]. However, application in pregnancy is limited (see Chap. 1). A low-dose CT scan is more sensitive than the renal US in locating urinary calculi during pregnancy [46].

#### 27.2.5.4 MR Urography

If the diagnosis is doubtful, MR urography is used. It is comparable to CT and requires safe and effective contrast media [47, 48]. Stones appear as storage defects, and at the same time, other causes of obstruction can be found, even outside the urinary tract.

#### 27.2.5.5 Intravenous Urography

Limited IV urography provides anatomic and functional information concerning the kidney [49]. Radiation exposure is reduced with a limited sequence, decreasing the exposure times, low voltages, tight collimation, maximal fetal shielding, and prone patient positioning [49].

### 27.2.6 Treatment

#### 27.2.6.1 Conservative Treatment

Medical management is often successful (64–84%) with IV hydration and pain medications [49–51]. Ureteral stones become symptomatic mostly in the mid-trimester, necessitating an

intervention [25, 52]. In nonpregnant patients, a spontaneous passage occurs in 68% with  $<5$  mm stone size and 47% with  $>5$  mm [53], whereas during pregnancy, the spontaneous passage rate is 70–80%, with 50% after delivery [49, 50, 54]. Spontaneous passage during pregnancy is higher partly due to physiologic ureteral dilatation. Because of the limitations in diagnostic methods, the rate of false-positive results is up to 23% [55]. Therefore, it is argued that the high spontaneous passage rate is due to a misdiagnosis. In a conservative approach, close follow-up is mandatory.

### Diet Therapy

Diet therapy follows the guidelines of the *American Urological Association* for the general population [38]:

- The fluid intake that will achieve a urine volume of at least 2.5 L daily,
- Limited sodium intake and consumption of 1–1.2 g/day of dietary calcium in patients with calcium stones and relatively high urinary calcium,
- Limited intake of oxalate-rich foods and maintenance of normal calcium consumption in patients with calcium oxalate stones and relatively high urinary oxalate,
- Increased intake of fruits and vegetables and limited nondairy animal proteins in patients with calcium stones and relatively low urinary citrate,
- Limited intake of nondairy animal proteins in patients with uric acid stones or calcium stones and relatively high urinary uric acid,
- Limited sodium and protein intake in patients with cystine stones.

### Pharmacologic Therapy

Diet therapy follows the guidelines of the *American Urological Association* for the general population [38]:

- Thiazide diuretics for patients with high or relatively high urine calcium and recurrent calcium stones,
- Potassium citrate therapy for patients with recurrent calcium stones and low or relatively low urinary citrate,

- Allopurinol for patients with recurrent calcium oxalate stones who have hyperuricosuria and normal urinary calcium,
- Thiazide diuretics or potassium citrate for patients with recurrent calcium stones in whom other metabolic abnormalities are absent or have been appropriately addressed, and stone formation persists,
- Potassium citrate for patients with uric acid and cystine stones to raise urinary pH to an optimal level,
- Allopurinol, but not as first-line therapy for patients with uric acid stones,
- Cystine-binding thiol drugs, such as  $\alpha$ -mercaptopyronylglycine (tiopronin), for patients with cystine stones unresponsive to dietary modifications and urinary alkalization or who have recurrent stones,
- Acetohydroxamic acid for patients with residual or recurrent struvite stones only after failed surgical options.

### Medical Expulsive Therapy

In addition to conservative treatment, the spontaneous passage rates can be increased with medical expulsive therapy (MET).  $\alpha$ -blockers and calcium channel blockers are safe during pregnancy [56].

Contraindications for MET and conservative treatment are [57]:

- Fever,
- Infection,
- Obstetric complications,
- Solitary kidney,
- Bilateral obstruction,
- Intractable pain,
- Oral intake problems,
- Stones >1 cm.

### 27.2.6.2 Surgical Treatment

Indications for surgical intervention are contraindications for conservative treatment. The most used procedures are percutaneous nephrostomy and ureteral stent placement. The disadvantage is temporary drainage with a need for definitive treatment.

### Ureterorenoscopy with Lithotripsy

A definitive treatment method, ureterorenoscopy, can be applied under spinal or general anesthesia. Safety and efficiency outcomes are similar in general and pregnant populations [58].

Contraindications for ureterorenoscopy are [58, 59]:

- Infection,
- Oversized stone,
- Complex anatomy,
- Bilateral obstruction,
- Obstetric complications,
- First trimester and near-term.

Ureteroscopy with Holmium laser has become the procedure of choice in pregnancy for symptomatic stones <1 cm without evidence of sepsis or history of the transplanted kidney. The Holmium laser has minimal penetration, 0.5–1.0 mm, making it well tolerated for surrounding tissue, and has decreased sound intensity compared with the US, negating fetal hearing damage [51].

### Percutaneous Nephrostomy

Temporary drainage with percutaneous nephrostomy immediately decompresses the obstruction without ionizing radiation and can be performed on patients with acute sepsis. It requires quick and minimal anesthesia, but it also has many disadvantages: bleeding during insertion, dislodgement, the social aspect of dealing with the device, and the necessity of multiple procedures because encrustation of the catheter is accelerated, requiring substitution every 4–6 weeks [49, 60, 61]. A percutaneous nephrostomy tube has a greater probability of infection and is more uncomfortable. If percutaneous nephrostomy has to be placed in an obstructed and infected system, a broad-spectrum antibiotic (ampicillin-sulbactam) is mandatory. In other cases, prophylaxis with a first-generation cephalosporin is indicated [62, 63].

### Ureteral Stents

Routine stenting after uncomplicated ureteroscopy in the general population is unnecessary. However,

a subgroup of patients could benefit from stent placement, evidenced by the higher hospital readmission rate. Pregnant patients should be included in this subgroup. The recommendation is to insert ureteral stents with pull-out strings to control early postoperative colicky pain for at least 72 h. Ureteral stents may be placed but are associated with increased lower urinary tract symptoms, may cause damage to the ureter during placement, and ultimately may encrust over, leading to obstruction. Classically, the decision to perform percutaneous nephrostomy versus stent placement depends on gestational age, with the former placed before 22 weeks and the latter afterwards. The opinion is that JJ stents are better tolerated since patients cannot view them. However, the disadvantages are lower urinary system complaints.

Rapid calcification and encrustation of ureteral stents placed during pregnancy occur in 75% [64]. Asymptomatic bacteriuria (ASB) during pregnancy can lead to rapid stent encrustation, especially by calcium phosphate and struvite stones. ASB is present when a urine culture from midstream collection contains one or more species of bacteria with a single isolate of >100,000 colony-forming units of an uropathogen. Also, hypercalciuria and hyperuricosuria seen during pregnancy might be the reason for rapid encrustation. Therefore, stents should be changed every 4–6 weeks [60, 61, 65]. Comparative advantages of percutaneous nephrostomy and ureteral stenting are in Table 27.2.

**Table 27.2** Comparative advantages of percutaneous nephrostomy and ureteral stenting

| Ureteral stenting                                                    | Percutaneous nephrostomy                        |
|----------------------------------------------------------------------|-------------------------------------------------|
| Catheters are not outside the body                                   | Catheters of different sizes (8–12 Fr)          |
| Lesser risk of hemorrhage                                            | The catheter can be irrigated                   |
| An interventional radiologist is not needed; any urologist can apply | Urine can be followed from the implanted kidney |
| No need for anesthesia                                               | Ureteral complications can be avoided           |
|                                                                      | Placement under local anesthesia                |

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27.2.7 Prognosis

Renal stones during pregnancy are associated with an increased risk of preeclampsia and UTI. Symptomatic nephrolithiasis results in a 1.4–2.4-fold increased risk of preterm labor [54, 66]. Also, urolithiasis increases the likelihood of low birth weight and CS. However, renal stones are not significantly associated with preterm rupture of membranes or infant mortality [26].

27.3 Acute Pyelonephritis

27.3.1 Incidence

UTI is more common during pregnancy [67]. ASB is present in 2–15% of pregnant women [68]. Symptomatic UTI, cystitis, and pyelonephritis complicate 1–2.5% of pregnancies [69–71]. It is similar to or slightly higher than in nonpregnant patients, but the progression to symptomatic bacteriuria or acute pyelonephritis is much higher during pregnancy [72]. In up to 35%, ASB may progress to symptomatic UTI or acute pyelonephritis. This rate is severalfold higher than in nonpregnant women [73]. UTI, unrelated to delivery, is the second most common reason for hospitalization during pregnancy [74]. While still common in developing countries, acute pyelonephritis during pregnancy has decreased substantially in developed countries.

Pyelonephritis in pregnancy occurs mainly before delivery, with 10–20% in the second and third trimesters [67, 75, 76].

UTI prevalence among pregnant women in Ethiopia, Sudan, and Tanzania is 15% [77–79]. A lower incidence is in Iran, Bangladesh, South Africa, Cameroon, and Saudi Arabia [80–85]. However, a higher incidence is in Egypt (32%), Pakistan (23.9%), and Libya (30%) [86–88].

**27.3.2 Etiopathogenesis and Risk Factors**

In pregnancy, urinary stasis and vesicoureteral reflux are caused by hormonal and mechanical changes [89]. The enlarging uterus can obstruct the ureters and compound urinary stasis, explaining why complicated pyelonephritis was seen more in the latter half of pregnancy [76, 90]. In addition, short urethra and difficulty with hygiene due to a distended pregnant belly increase the rate of UTI [80]. Furthermore, immunological suppression during pregnancy makes the mother an immunocompromised host [91]. These changes increase the risk of symptomatic and asymptomatic UTI even in healthy pregnant women [92]. During pregnancy, anatomical and physiological changes in the urinary tract increase the risk of urolithiasis (see Sect. 27.1.3), which increases the likelihood of UTI. Also, ASB increases the risk of acute pyelonephritis by 20- to 30-fold in pregnant women compared to women without ASB [67]. The delivery trauma may induce bladder hypotonicity. Frequent catheterization is often necessary and represents an additional risk factor. Among pregnant women with acute pyelonephritis, 9–17% were found to have concurrent bacteremia [70, 93, 94]. Notably, 3–5% of acute pyelonephritis cases are associated with diabetes mellitus [70, 95], a known UTI predisposition. Risk factors for UTI and acute pyelonephritis are summarized in Table 27.3.

**Table 27.3** Risk factors for acute pyelonephritis in pregnancy [71, 72, 77, 89, 95–98]

| Proven                           | Questionable               |
|----------------------------------|----------------------------|
| Urinary stasis                   | Multiparity                |
| Urinary tract malformations      | History of catheterization |
| Low socioeconomic status         | Gestational age            |
| Asymptomatic bacteriuria         | Delivery trauma            |
| Hispanic or Black                |                            |
| American Indian or Alaska Native |                            |
| Age <29 years                    |                            |
| Diabetes mellitus                |                            |
| Sexual activity                  |                            |
| History of UTI                   |                            |
| Vitamin D deficiency             |                            |
| Proteinuria                      |                            |

Despite increased adherence to guidelines recommending routine screening for ASB in pregnancy, other age-related comorbidities may increase the risk for acute pyelonephritis. Multiparity is a questionable risk factor because it was confirmed only in low-income countries like Nigeria, Iran, Pakistan, and Ethiopia [77, 89, 99, 100]. The association between multiparity and UTI is due to physiologic changes affecting the urinary tract during multiple pregnancies. These changes are more likely in successive pregnancies. Furthermore, repeated childbirth trauma to the female urethra could make it prone to UTI. UTI during pregnancy is frequently associated with hypertensive disorders, increasing the risk of perinatal morbidity. Calcitriol, vitamin D3’s most active metabolite, regulates blood pressure and prevents UTI, partially through modulating vasoactive peptides and antimicrobial peptides, like cathelicidin. Vitamin D deficiency might predispose to maternal cardiovascular risk and perinatal infections, especially in male-carrying pregnancies, partly due to lower placental CYP27B1 and cathelicidin expression [96].

In the same pregnancy, pregnant women have a 15–20% risk of developing recurrent pyelonephritis [70, 76]. This risk is 60% without suppressive therapy after the completion of antibiotic therapy [76].

**27.3.3 Screening**

Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the *Infectious Diseases Society of America* made the following recommendations [67]:

- In pregnant women, we recommend screening for and treating ASB (strong recommendation, moderate-quality evidence). We suggest a urine culture collected at one of the initial visits early in pregnancy. There is insufficient evidence to inform a recommendation for or against repeat screening during pregnancy for a woman with an initial negative screening culture or following treatment of an initial episode of ASB;

- We suggest 4–7 days of antimicrobial treatment in pregnant women with ASB rather than a shorter duration (weak recommendation, low-quality evidence). The optimal duration of therapy will vary depending on the antimicrobial given; the shortest effective course should be used.

Maternal colonizing ESBL strains are a risk factor for neonatal colonization and sepsis with these organisms [101, 102]. Screening and treating ASB in pregnancy reduce the risk of subsequent pyelonephritis from 20–35% to 1–4% [75]. ASB is diagnosed by urine culture or high-throughput DNA sequence-based analyses [92]. The dipstick test has a very low sensitivity (4.5%) with an absolute (100%) specificity for nitrites [85]. The leucocyte esterase has a low sensitivity (48.3%) and specificity (44.9%) [85]. Gram-positive organisms do not reduce nitrate to nitrite in urine, so the lower nitrite sensitivity as a screening test is understandable. Also, leukocyturia cannot solely be attributed to UTI since other sexually transmissible infections, such as *C. trachomatis*, also cause leukocyturia [85].

### 27.3.4 Clinical Presentation

Symptoms of acute pyelonephritis include fever ( $>38^{\circ}\text{C}$ ), chills, nausea, vomiting, and flank pain with or without the cystitis symptoms of painful, frequent, or urgent urination. Physical examination shows findings of fever and costovertebral angle tenderness. Isolated asymptomatic frequency ( $\geq 7$  daytime voids) or nocturia is mostly physiologic. The physiological frequency is 59% in early pregnancy, 61% in mid-pregnancy, and 81% in late pregnancy [103]. Fever remains an important clinical criterion for diagnosing pyelonephritis, although it may be absent at presentation [104].

Acute pyelonephritis is the leading cause of septic shock during pregnancy [105].

### 27.3.5 Differential Diagnosis

The difference in the sequence of events in acute appendicitis and acute pyelonephritis is diagnostic. In acute appendicitis, the pain starts first, later fever, and rarely chills. In pyelonephritis, chills come first, then fever, and pain (see Sect. 15.6.4).

### 27.3.6 Diagnosis

The UTI cannot be excluded without nitrites in the urine (see Sect. 27.3.3). Single negative urinalysis does not exclude UTI. Repeated urinalyses confirm bacteriuria or pyuria. An antibiogram is mandatory because the same bacteria were sensitive to different antibiotics in different studies [85].

Compared to white blood cell (WBC) counts, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) level, serum procalcitonin levels are valuable in differentiating acute pyelonephritis from ASB and acute cystitis in pregnancy [106].

A procalcitonin value of  $>0.25$  ng/ml for diagnosing acute pyelonephritis has a sensitivity of 87% and a specificity of 79% [106].

The utility of blood cultures in managing acute pyelonephritis in pregnancy is inefficient. Only 1.3% of pregnant [107] and 1.3% of non-pregnant female patients [94] had blood cultures with pathogens that differed from those found in the urine.

The most common associated finding with acute pyelonephritis in pregnancy is anemia in 22–25% [70, 71, 95].



## 27.3.7 Treatment

### 27.3.7.1 Conservative Treatment

The South African Essential Drug List (2020) recommends empiric nitrofurantoin 100 mg 6 h for 5 days or a single 3 g dose of fosfomycin to treat acute cystitis in pregnancy [108].

With the risk of severe complications from acute pyelonephritis during pregnancy, particularly in the latter half of gestation, hospitalization is generally recommended for treatment and monitoring [109]. *E. coli* is the most common uropathogen associated with acute pyelonephritis [70, 75, 110]. The top three pathogens remained consistent: *E. coli*, *E. faecalis*, and *K. pneumoniae* [68]. Other common microorganisms include *Proteus* spp., and Gram-positive microorganisms, such as *S. aureus*, *S. saprophyticus*, group B Streptococcus, and *Enterococcus* spp. [76]. The most commonly used antibiotics are presented in Table 27.4. The duration of antibiotic treatments and maintenance therapy is rarely specified [76]. While the high *E. coli* susceptibility rates to nitrofurantoin and fosfomycin remained stable, a significant increase in ESBLs was seen. Similarly, the ESBL rate and emergence of carbapenem resistance in the *K. pneumoniae* isolates are issues. Ampicillin susceptibility of *E. faecalis* is high. Amoxicillin-clavulanate demonstrated high activity levels against the top three uropathogens [68].

The South African Essential Drug List (2020) recommends ceftriaxone as empiric therapy for pyelonephritis in pregnancy [108].

Pregnant patients with acute pyelonephritis are more susceptible to complications compared to nonpregnant adults, especially ARDS and the

need for mechanical ventilation [70, 90]. Extracorporeal membrane oxygenation is rescue therapy for ARDS from acute pyelonephritis (see Sect. 2.1.4). Approximately 0.5% of pregnant women have recently been hospitalized for acute pyelonephritis [71], less than previously reported [112]. Implementing the guidelines for screening for ASB in pregnancy by the *US Preventative Health Task Force* and the *American College of Obstetricians and Gynecologists* may be partly responsible. It is also possible that the high rates of early entry into prenatal care and the population characteristics might have contributed to the observed low rate. The average hospital stay is <3 days [95, 112]. This reflects the recommendation for hospitalization and administration of IV antibiotics until the patients remain afebrile for at least 24–48 h. There is no difference in the length of hospital stay between trimesters [113].

The severity of acute pyelonephritis, not gestational age, determines the duration of hospitalization.

The obstetric-specific maternal early warning criteria have been to detect patients with abnormalities in clinical parameters associated with severe maternal morbidity and mortality, including sepsis (Table 27.5).

Decisions to change initial antibiotic regimens are more affected by clinical course than blood culture results (see Sect. 27.3.6). Antibiotics other than nitrofurantoin or sulfamethoxazole-trimethoprim for lower UTI in pregnancy were not associated with an increased progression to acute pyelonephritis, preterm labor, or low birth weight [114].

### 27.3.7.2 Obstetric Management

Most women, including those with a more aggressive course, deliver at term. Immediate delivery with acute pyelonephritis is not always indicated, especially if fetal monitoring has been reassuring [76].

**Table 27.4** Preferred antibiotics for treatment of urinary tract infection and pyelonephritis in pregnancy [111]

| Drug                      | Mode of administration | Dosage                                | Comments                                                                                                              | FDA category |
|---------------------------|------------------------|---------------------------------------|-----------------------------------------------------------------------------------------------------------------------|--------------|
| <b>Penicillins</b>        |                        |                                       |                                                                                                                       |              |
| • Amoxicillin             | Oral                   | 500 mg every 8 h or 875 mg every 12 h | Give 3–7 days<br>May have limited utility against gram-negative organisms                                             | B            |
| • Ampicillin              | Oral                   | 250–500 mg every 6 h                  | Give 3–7 days<br>Commonly used                                                                                        | B            |
| • Piperacillin-tazobactam | IV                     | 3.375 g every 6 h                     | Give 7–14 days for severe infection                                                                                   | B            |
| <b>Cephalosporins</b>     |                        |                                       |                                                                                                                       |              |
| • Cephalexin              | Oral                   | 500 mg every 6 h                      | Give 3–7 days<br>Commonly used                                                                                        | B            |
| • Cefpodoxime             | Oral                   | 100 mg every 12 h                     | Give 3–7 days                                                                                                         | B            |
| • Ceftriaxone             | IV                     | 1 gm every 24 h                       | Give 7–14 days<br>Commonly used                                                                                       | B            |
| • Cefepime                | IV                     | 1 gm every 12 h                       | Give 7–14 days<br>Covers <i>Pseudomonas</i>                                                                           | B            |
| <b>Monobactam</b>         |                        |                                       |                                                                                                                       |              |
| • Aztreonam               | IV                     | 1 g every 8 h                         | Give 7–14 days in setting of beta lactam allergy                                                                      | B            |
| <b>Carbapenems</b>        |                        |                                       |                                                                                                                       |              |
| • Imipenem/cilastatin     | IV                     | 500 mg every 6 h or 1 g every 8 h     | Give 7–14 days<br>Limited data; for severe infection                                                                  | C            |
| • Meropenem               | IV                     | 1 g every 8 h                         | Give 7–14 days<br>Limited data; for severe infection                                                                  | B            |
| <b>Nitrofurans</b>        |                        |                                       |                                                                                                                       |              |
| • Nitrofurantoin          | Oral                   | 100 mg every 12 h                     | Give 5–7 days<br>Common prophylactic agent; avoid in G6PD deficiency and third trimester for risk of hemolytic anemia | B            |

FDA Food and Drug Administration, G6PD deficiency glucose-6-phosphate dehydrogenase deficiency

**Table 27.5** Maternal early warning criteria

|                                                                                                                               |             |
|-------------------------------------------------------------------------------------------------------------------------------|-------------|
| Systolic blood pressure (mmHg)                                                                                                | <90 or >160 |
| Diastolic blood pressure (mmHg)                                                                                               | >100        |
| Heart rate (beats per min)                                                                                                    | <50 or >120 |
| Respiratory rate (breaths per min)                                                                                            | <10 or >30  |
| Oxygen saturation on room air, at sea level, %                                                                                | <95         |
| Oliguria, mL/h for $\geq 2$ h                                                                                                 | <35         |
| Maternal agitation, confusion, unresponsiveness or unrelenting headache, or shortness of breath in patients with preeclampsia | –           |

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## 27.3.8 Prognosis

### 27.3.8.1 Maternal Outcome

Pregnant women who had delayed diagnosis or less aggressive management had worsening RDS requiring mechanical ventilation, worsening anemia requiring blood transfusion, or worsening renal dysfunction requiring dialysis [76]. Nearly one-quarter of affected women will have  $\geq 1$  recurrence during pregnancy [90]. Admission vital signs may not reliably identify women with pyelonephritis at risk of adverse maternal outcomes. Maternal adverse outcomes are more

likely with leukocytosis, thrombocytosis, bacteremia, and abnormal serum potassium [115]. Gestational age at diagnosis of acute pyelonephritis does not influence maternal outcomes [71, 76]. There was no difference in ICU admission rates or ARDS rates between patients with a fever and those without a fever [104]. However, all patients who required ICU admission and developed ARDS had pyrexia during hospitalization.

Maternal complications include anemia in 23–66%, sepsis in 30–60%, renal dysfunction in 20%, and 2–8% for acute respiratory distress syndrome (ARDS). The current study found 0.5% of ARDS with acute pyelonephritis [71]. Contrary to previous reports [116], the most common uropathogen identified in women with ARDS and pyelonephritis was *E. coli*, not *K. pneumoniae* [71]. Histamine, bradykinins, and a cascade of proinflammatory cytokines can trigger severe lung disease or septic shock [117]. Antepartum diagnosis of sepsis/septicemia from acute pyelonephritis was present in 12–17% [70, 118]. An increased risk for endometritis and mastitis postpartum was found in women with symptomatic lower UTI during pregnancy [119].

The exact risk of preterm labor and delivery directly attributable to acute pyelonephritis in pregnancy is difficult to estimate. The delivery may not occur during the admission for the acute disease, and the risk factors for pyelonephritis and preterm delivery overlap [120]. Acute pyelonephritis in pregnancy leads to a modestly higher (10.3% vs. 7.9%) [71] to a significantly higher (5% vs. 1%) [70] likelihood of preterm delivery. An additional factor for increased risk is the higher incidence of pyelonephritis in the second half of pregnancy. The threat of preterm delivery can result in tocolytic administration, compounding the risk of pulmonary edema and respiratory insufficiency [116].

Women with acute pyelonephritis are at increased risk for preterm delivery [71, 76].

### 27.3.8.2 Fetal Outcome

Even though maternal UTI has few direct fetal sequelae from fetal bloodstream infection, uterine hypoperfusion due to maternal dehydration, maternal anemia, and direct bacterial endotoxin damage to the placental vasculature may cause fetal cerebral hypoperfusion [121]. Urosepsis may be related to an increased cerebral palsy rate among preterm infants. Whether urosepsis, toxins, fetal infection, or maternal febrility cause cerebral palsy remains unknown (see Chap. 4).

Pregnant women with acute pyelonephritis are more likely to have premature delivery and low birth weight [71, 122, 123]. Also, pregnant women with ASB seemed more likely to result in premature delivery or low birth weight. Gestational age at diagnosis of acute pyelonephritis does not influence fetal outcomes [71, 76].

A recommendation is to treat asymptomatic bacteriuria in pregnancy [67, 124], although the relationship between asymptomatic bacteriuria and preterm delivery is unclear [71].

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# Urinary Tract Obstruction or Rupture

# 28

## Abstract

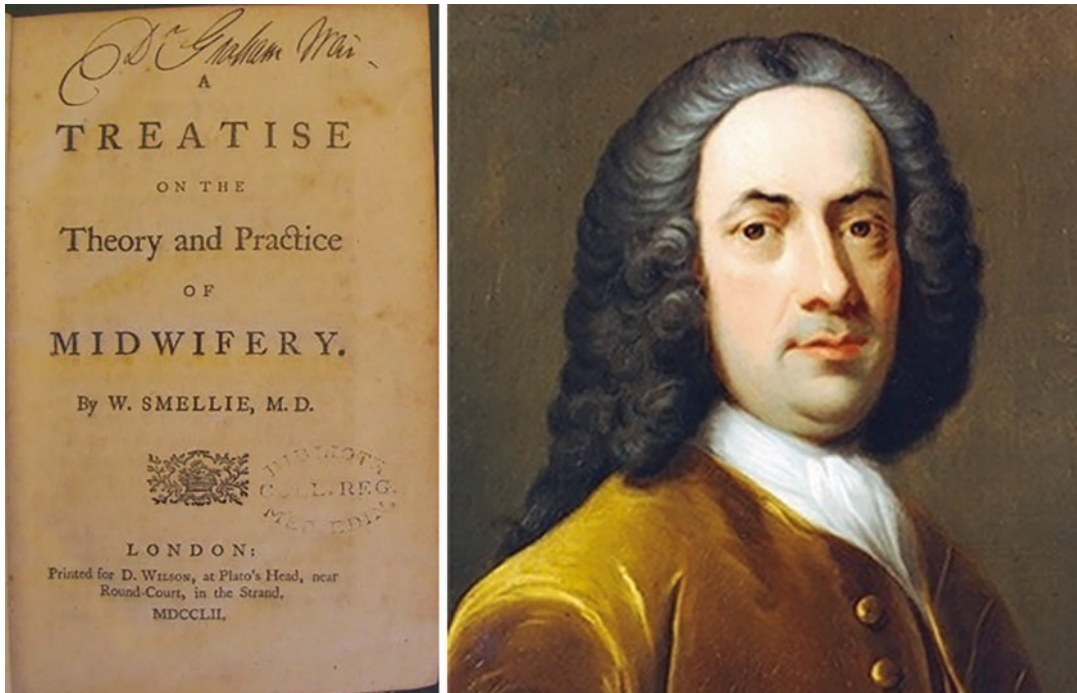
During advanced pregnancy, the urinary bladder is compressed at its dome, increasing intravesical pressure. Ureteric dilation is physiologic in pregnancy, with right-sided predominance (80%). Urolithiasis results from the anatomical and physiological changes in the urinary system during pregnancy, including changes in the chemical properties of urine. Diagnosis is mostly by transabdominal ultrasound. In uncertain cases or when more details, such as level and cause of obstruction, are needed, MR urography is done. The treatment is usually nonoperative. Failure of nonoperative methods indicates surgical treatment, such as ureterorenoscopy with lithotripsy, percutaneous nephrostomy, and JJ placement. Acute urinary retention is more frequent after delivery and is treated with Foley's urethral catheterization. The retroverted uterus should be repositioned. Manual reposition has a high success rate. Bladder rupture can be spontaneous or related to pregnancy and delivery. Acute urinary retention is common due to a retroverted uterus in the

ninth and 16th gestational week. Foley urinary catheter placement or manual reposition is therapeutic. Without treatment, it leads to bladder rupture. Another cause of bladder rupture is blunt abdominal trauma, while bladder injury occurs during Cesarean section.

## 28.1 Acute Urinary Retention

### 28.1.1 Historical Perspective

Alfred McClintock published a book based on William Smellie's (Fig. 28.1) work in 1876 and reported complete urinary retention in the fourth month of pregnancy [3]. R.G. McKerron, in 1902 realized that urinary retention after labor, without eclampsia, is not so uncommon [4]. J. Barris, in 1912, reported a case of overdistension of the bladder resulting in hematuria [5]. Granville E Crabtree (Boston Lying-In Hospital), in 1942, described the third [6], while Burdon et al., in 1951, described the fourth patient [7], all in the fourth month of gestation. In all cases, maximal retroflexion prevented the rise of the uterus out of the pelvis.



**Fig. 28.1** William Smellie (Feb 5, 1697, Lanark–Mar 5, 1763, Lanark) was a Scottish obstetrician and medical instructor. Having started as an apothecary and a surgeon, Smellie began his practice in Lanark in 1720, later moving to London. (a) One of the first prominent male midwives in Britain, he designed an improved version of the obstetrical forceps, established safer delivery practices,

and helped make obstetrics more scientifically based through his teaching and writing. He is often called *the father of British midwifery*. (Reproduced with permission from the Royal College of Physicians of Edinburgh [1]. (b) This is thought to be a self-portrait (1719) that hangs in the Royal College of Surgeons of Edinburgh [2])

### 28.1.2 Incidence

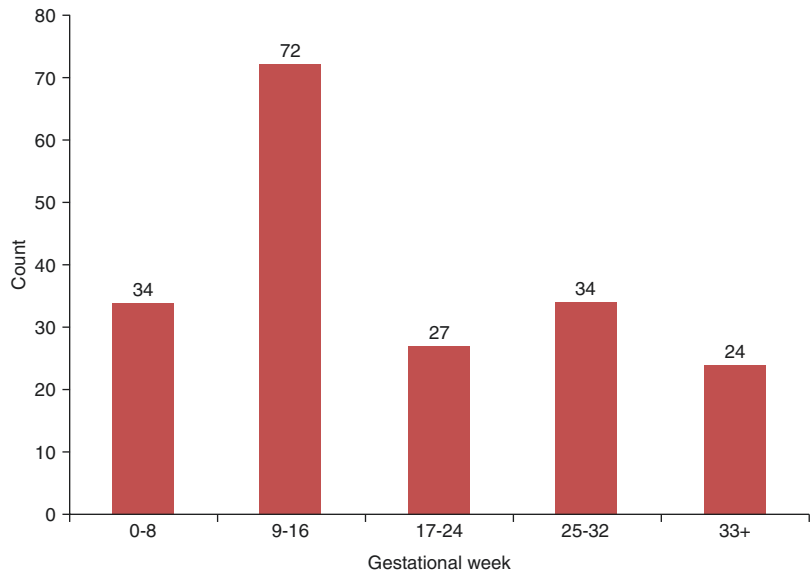
Due to different definitions, it is difficult to estimate acute urinary retention (AUR). Therefore, the incidence varies largely, from 0.5 to 51.7% [8, 9]. The largest studies claim an incidence of 0.1–0.47% [10]. Claimed postoperative AUR incidence is around 0.05–0.06% [8, 11].

The most common period for AUR during normal pregnancies is between the ninth and 16th gestational week (66% during the first trimester [12]), although it is present throughout pregnancy (Fig. 28.2). This gestational distribution correlates with the incidence of the retroverted uterus as the most common cause of AUR in pregnancy. In early pregnancy, the incidence of the retroverted uterus is 11–20% [13, 14], although the incidence of AUR due to a

retroverted uterus is only 1.4% [14] or 1/3000 pregnancies [15]. AUR from the incarcerated retroverted uterus in the English literature up to 1995 revealed only 27 cases [16]. Of 35 cases between 1980 and 2018, most were due to incarcerated or retroverted uterus [17]. Fewer than 30 cases of bladder cancer during pregnancy have been described [18, 19], and not a single one presented with AUR. A retroverted uterus is a cause in 15–33.3%, lower genital infection in 26.7%, while in 40%, the cause was unknown [12].

*Overt postpartum AUR* is the inability to void spontaneously within 6 h after vaginal delivery or 6 h after removing an indwelling catheter (IDC). *Covert postpartum AUR* is a postvoid residual bladder volume of >150 ml after spontaneous voiding.

**Fig. 28.2** Frequency of the first acute urinary retention episode in normal pregnancies by 8-week gestational intervals. (Reproduced with permission from [10])



### 28.1.3 Etiopathogenesis

#### 28.1.3.1 Pregnancy

Some risk factors include an incarcerated uterus, or cervical pregnancy [20], though most women have no antepartum risk factors [10]. A risk factor is a maternal age over 35 years [10]. AUR in a previous pregnancy suggests susceptibility to retention, though the causative mechanism is unclear [21].

#### Retroverted Uterus

As the uterus enlarges during the first trimester, the fundus rises typically from the hollow of the sacrum to an anterior ventral position, spontaneously correcting any retroversion before 14 weeks of gestation. Eccentric hypertrophy occurs when the anterior wall undergoes more rapid distention than the posterior wall and, emerging above the superior strait, eventually draws up the rest of the uterus. When the uterus fails to ascend into the abdominal cavity (sometimes adhesions from pelvic inflammation trap the uterine fundus within scar tissue), the fundus becomes wedged below the sacral promontory, where it continues to enlarge [15]. The cervix becomes displaced cephalad against or above the symphysis pubis, causing compression of the urethra and bladder neck [22], which interferes with normal voiding (Fig. 28.3).

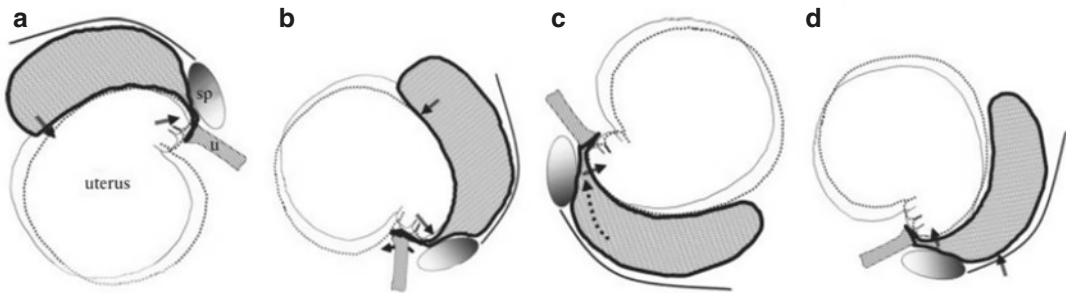
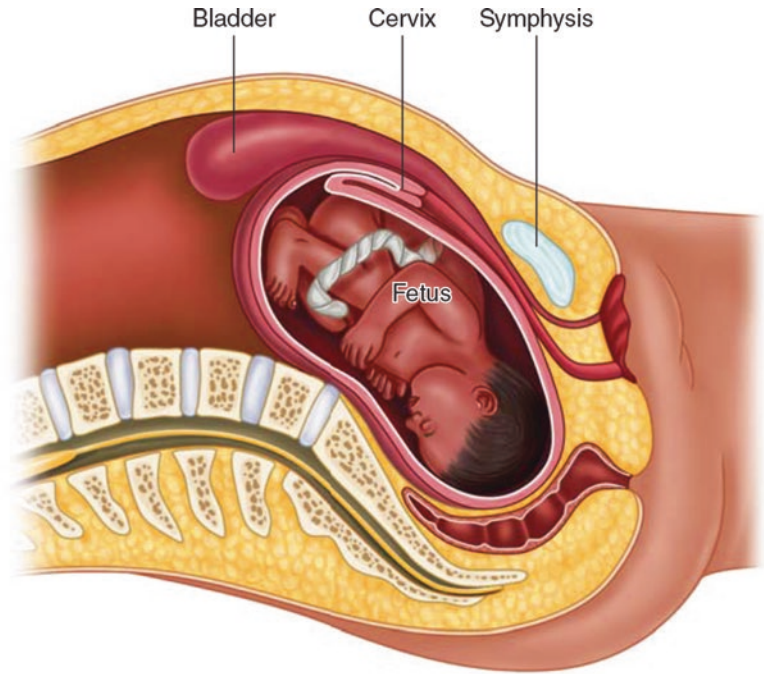
During the day, bladder irritation leads to dysuria and urination frequency prevents bladder distension. When the patient waits too long before urinating, urine accumulates in the lower part of the bladder creating differences in pressure between the bladder and the urethra, which permit spontaneous urination, protecting the bladder against distension [24]. In the erect position, trying to void may be similar to unplugging a sink full of water. The more water in the sink, the more pressure it exerts on the plug, and the more difficult it is to pull it. The Valsalva maneuver adds further pressure on the impacted uterus, leading to further lower bladder compression [24].

In contrast, when the patient is supine, the upper part of the bladder becomes dependent on bladder filling for urination. The differences in pressure between the bladder and the urethra are greatly diminished, favoring the accumulation of urine in the bladder without the urge for emptying (Fig. 28.4). This anatomic change further disturbs the pressure ratio allowing spontaneous bladder emptying and thus leads to AUR. This phenomenon explains the higher frequency of AUR during the night or when the patient awakens in the morning [24, 25].

Conditions that may inhibit the fundus of the enlarging uterus from ascending out include adhesions related to previous pelvic surgery,



**Fig. 28.3** Illustration of an incarcerated uterus at term. Notice the elongated vagina with the uterine fundus and the fetal head impacted deep in the pelvis. (Reproduced with permission from [23])



**Fig. 28.4** Schematic diagram displaying the presumptive vectors of mechanical pressure (*solid arrows*) acting on the lower urinary tract in the (a) supine position, (b) during a Valsalva maneuver in the sitting position, (c) in the prone position, and (d) during a Credé's maneuver with body trunk leaning forward in the sitting position. Solid

and dotted lines indicate the uterine position before and after, respectively, a change of body position/performing maneuver; a *dotted arrow* indicates the reopening of the lower bladder. *sp*, pubic symphysis; *u*, urethra. (Reproduced with permission from [24])

pelvic inflammatory disease, endometriosis, large fibroids, uterine malformation, a deep sacral concavity with an overhanging promontory or laxity of the supporting tissues [26, 27]. Incarceration can also occur in the absence of predisposing factors [28, 29]. Why so few patients develop this complication is unclear,

but AUR can result from other factors besides the retroverted uterus. In addition to AUR, other complications can be (simultaneously) present. The retroverted uterus results in an almost doubled incidence of spontaneous abortion in early pregnancy [14].

### Uterine Fibroids

The posterior intramural fibroid is prone to retroversion. This is exaggerated in pregnancy due to the increasing vascularization of the uterus and fibroid growth. Consequently, if the fibroid is in a posterior and lower or isthmic position, it can promote incarceration of the uterus or become incarcerated in the pelvic cavity [25].

### Other

Several other risk factors increase the risk of AUR (Table 28.1); some are interrelated and may even promote each other [11]. Instrumental birth may be confounded by other factors such as prolonged labor, epidural analgesia, parity, and episiotomy, making it questionable whether it is an independent predictor [30]. Previous delivery has a protective effect against AUR [10] while increasing the risk of stress urinary incontinence, unlike AUR. Association between preterm delivery and AUR is undefined. Probably, women with preterm delivery have more gynecological or fetal illnesses than women with a normal pregnancy [10].

**Table 28.1** Causes of acute urinary retention during pregnancy [10, 11, 30–32]

| Local                               | Systemic                      | Postpartum                  |
|-------------------------------------|-------------------------------|-----------------------------|
| Retroverted uterus                  | Opioid analgesia              | Previous abortion           |
| Uterine myoma                       | High-dose regional anesthesia | Pelvic abnormality          |
| Threatened miscarriage              | Overweight mother             | Disproportion               |
| Placenta previa                     |                               | Endometriosis               |
| Third/fourth-degree perineal trauma |                               | Urinary tract infection     |
| Instrumental delivery               |                               | Pelvic or genital infection |
| First and second stage >10 h        |                               | Genital herpes              |
| Second stage >60 min                |                               | Kristeller Maneuver         |
| Nulliparity                         |                               | Mediolateral episiotomy     |
| Fetal head circumference of >36 cm  |                               | Vaginal delivery after CS   |
| Ectopic pregnancy                   |                               | Preterm delivery            |

### 28.1.4 Postpartum

Postpartum AUR has no standard definition. In 2001, Calgary Health Region's Policy and Procedures outlined postpartum AUR as the catheterization of the bladder within the first 24 h postpartum for not voiding within 6 h postpartum, often micturate in small amounts, or having the urge to micturate but cannot or to be catheterized for any reason for an amount of 500 ml output within the first 24 h postpartum [33]. In 2003, the *International Continence Society* defined the condition as a painful, palpable, or percussive bladder in a patient who cannot pass urine [34]. For example, pain may not be a presenting feature after regional anesthesia.

Yip et al.'s classification of postpartum AUR [32]:

- *Overt*: unable to void within 6 h of the delivery and require catheterization to drain a urinary volume greater than normal bladder capacity (400–600 ml),
- *Covert*: unable to pass more than 50% of normal bladder capacity or postvoid residual volume is >150 ml.

Vaginal delivery can cause major m. levator ani defects, predisposing women to pelvic floor dysfunction [35]. However, whether the muscle defect results from the rupture or neurologic or ischemic damage is unknown. Perineal trauma is certainly the primary cause of its damage. Mechanical strength applied to the pelvic muscles floor during instrument-assisted delivery, and the rise in abdominal pressure during Kristeller's maneuver, may contribute to pelvic and pudendal nerve damage. This leads to a loss of balance between detrusor contraction and urethral relaxation and consequent impairment of normal micturition, bladder overdistension, and AUR [32, 36]. The second-degree perineal tear (3.42×) and episiotomy (1.37×) [37], primarily mediolateral [38], increase the risk of AUR.

Many obstetrical risk factors contribute to postpartum AUR. (High-dose) regional analgesia could cause temporary disruption of afferent input. AUR related to instrument-assisted vaginal delivery is related to impaired reflex and voluntary relaxation of the urethral sphincter, periurethral muscles, and pelvic floor. In addition to its neurologic effects, instrument-assisted delivery may result in mechanical obstruction due to perineal edema, or it may cause direct bladder trauma. By prolonging the second stage of labor, regional analgesia may be associated with bladder overdistention and increased local edema [32]. Epidural analgesia during labor may increase AUR risk by up to three times [31].

Obstetric risk factors associated with postpartum AUR are presented in Table 28.1.

None of the patients with antenatal AUR developed postpartum AUR, suggesting that the causes of antenatal AUR are not the same as those for postpartum AUR [21].

## 28.1.5 Clinical Presentation

### 28.1.5.1 Medical History

The retroverted uterus causes nonspecific and general urinary symptoms like dysuria, overflow urinary incontinence, urinary frequency (more common in exaggerated uterine anteversion due to pressure on the bladder), and urinary infection (painful urination and frequency) in early pregnancy. The symptoms are due to the pressure of the retroverted uterus to the adjacent pelvic organs, also causing tenesmus, abdominal pain, and swelling of the lower extremities as a result of compression of the common iliac veins [15]. Vaginal spotting or frank bleeding in the early stages of pregnancy is also common [14]. However, if the retroverted uterus remains undiagnosed and pregnancy advances, it can cause severe obstetric and nonobstetric complications, including AUR [39].

Usually, AUR due to a retroverted uterus occurs before 20 weeks (found in all trimesters but most commonly between tenth and 16th week) of gestation and presents with suprapubic pain and inability

to void. Sometimes the patient attempts voiding in various positions without success [20].

Clinical suspicion of postpartum AUR is evident in patients with small voided volumes, urinary frequency, slow or intermittent stream, urgency, bladder pain or discomfort, urinary incontinence, and those who strain to void or describe no sensation to void [40]. While overt forms are easily diagnosed, covert ones are often underestimated because many patients may not report obvious urinary symptoms. Therefore, prompt diagnosis and adequate recognition are important [32].

### 28.1.5.2 Physical Examination

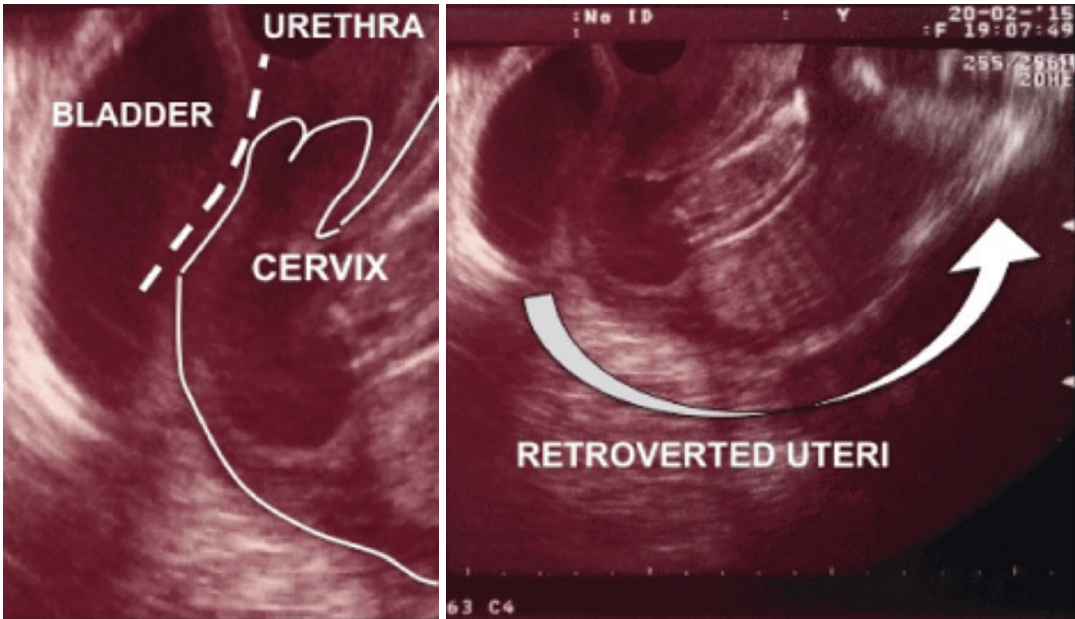
AUR during pregnancy is an emergency and presents as lower abdominal pain with a palpable bladder. Pelvic examination reveals a severely retroflexed uterus with an anterior cervix and superiorly displaced urinary bladder. The cul-de-sac is filled with the softly enlarged uterus bulging into the vagina. As a cause of AUR, uterine myomas are difficult to palpate [25]. Other abnormalities should be excluded, such as urinary tract infection (UTI), bladder stone, cystocele and rectocele, excessive fluid intake, constipation, medication, fibroid uterus, or pelvic tumor.

## 28.1.6 Differential Diagnosis

AUR is easy to diagnose clinically, but the cause of AUR should be defined. If systemic causes are excluded (hypovolemia, bleeding, or sepsis), a local cause should be found. Delay in the diagnosis of uterine incarceration can lead to other complications that can even mask AUR. These include fetal loss (up to 33%), infection, uterine rupture, vascular obstruction, ureteral obstruction, bladder ischemia, bladder rupture, or rectal gangrene. Other complications during the pregnancy include preterm labor, intrauterine growth restriction, labor dystocia, and difficulty with hysterotomy at the time of Cesarean section (CS) [15, 41, 42].

### 28.1.7 Diagnosis

Inserting a Foley urethral catheter confirms AUR with urine volume higher than normal bladder capacity ( $\approx 900$  ml when the retroverted uterus is



**Fig. 28.5** Transvaginal ultrasound shows a retroverted uterus during pregnancy. The cervix lies posteriorly to the urinary bladder, and the uterus normally extends superiorly

from it, but the direction of the body of the fetus reveals that the uterus extends backward. (Reproduced with permission from [48] under the CC Attribution License)

the cause [24, 43]), which abruptly relieves suprapubic pain. Further diagnostics define the cause of AUR. Delay in AUR diagnosis can result in irreversible uterine ischemia with spontaneous abortion, rupture of the uterus or bladder, rectal gangrene, and infection of uterine contents [44].

Urinary symptoms in pregnancy do not correlate with urodynamic findings, although the number of patients are small [45]. Urinary symptoms change throughout pregnancy [46], so urodynamics is unlikely to add significant information when treating women with antenatal AUR [21].

#### 28.1.7.1 Laboratory Findings

When a pregnant woman presents with symptoms of UTI with negative urine culture, a pelvic examination should exclude retroverted uterus compressing the urethra. If AUR is detected due to the retroverted uterus, postvoid urine volume should be controlled, resolving the symptoms [47]. Urinalysis from urine specimens during urethral catheterization excludes urinary tract infection as an underlying cause.

#### 28.1.7.2 Transvaginal Ultrasound

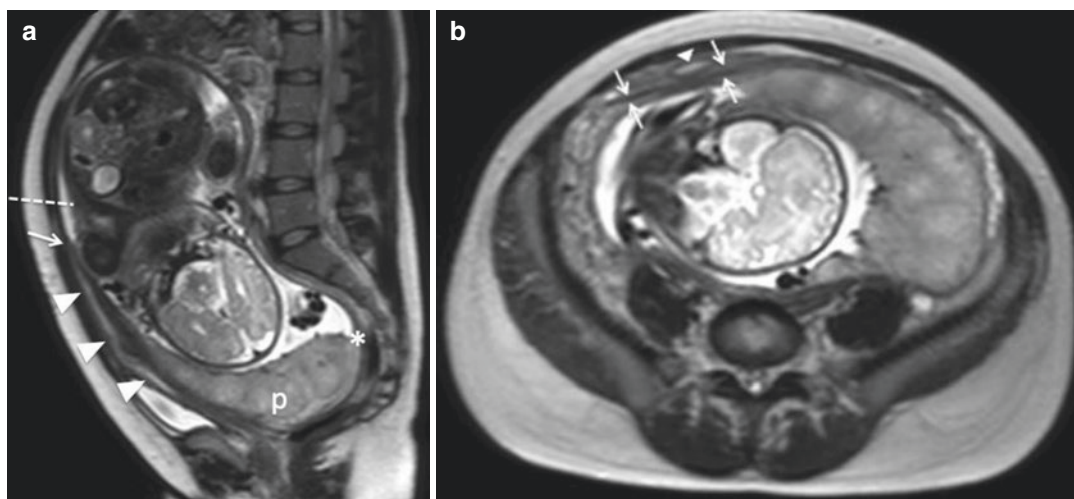
The first imaging method for defining the bladder status and delineating the cause of AUR is a



**Fig. 28.6** Transabdominal ultrasound reveals a single live intrauterine pregnancy within a markedly retroverted and likely incarcerated uterus, as evidenced by the abnormal position of the cervix relative to the uterine body (white arrow). The placenta is anteroposterior (star). (Reproduced with permission from [49])

transvaginal ultrasound (US). It can show a retroverted uterus (Fig. 28.5) or uterine fibroid, causing either retroversion or direct urinary bladder compression. A retroverted uterus pushes the cervix against pubic symphysis with obscured borders (Fig. 28.6). 3D mode more accurately defines these borders. During the Valsalva maneuver, there is no limitation on urethral mobility. The descent of the bladder neck is of rotational type with urethral mobility





**Fig. 28.7** Abdominal MR of the incarcerated uterus at 34 weeks of gestation. **(a)** Sagittal view, T2-weighted, shows an extremely elongated cervix (*arrowhead*). The incarceration of the uterus (\*), including the fetal head and placenta (*p*), in the pouch of Douglas. This view shows the placenta placed in the posterior wall of the uterus and has sufficient margins from the internal cer-

cal os (*arrow*). The level of the hysterotomy is indicated by the dotted line (...), located above the internal os to avoid cervix and posterior uterine wall injuries. **(b)** Low T2 signal intensity (*arrows*) behind the cervix showing the space between the cervix and posterior uterine wall in the axial view. (Reproduced with permission from [50] under the CC BY 4.0)

around 80°. The cervix compresses the lower bladder (not the adjacent proximal urethra) to the point that it overlays the internal urethral orifice. The compression could be such that the urine cannot be visible in that bladder portion.

### 28.1.7.3 Abdominal MR

Abdominal MR is the imaging modality of choice for diagnosing the incarcerated uterus and fetal morphology (Fig. 28.7).

### 28.1.7.4 Cystoscopy

A thorough investigation of the lower urinary tract is mandatory, including cystoscopy, in pregnant patients with a retroverted uterus who develop AUR [51], although compression is almost always external.

The concomitant bladder pathology is rare, including bladder cancer with AUR due to the retroverted uterus [51].

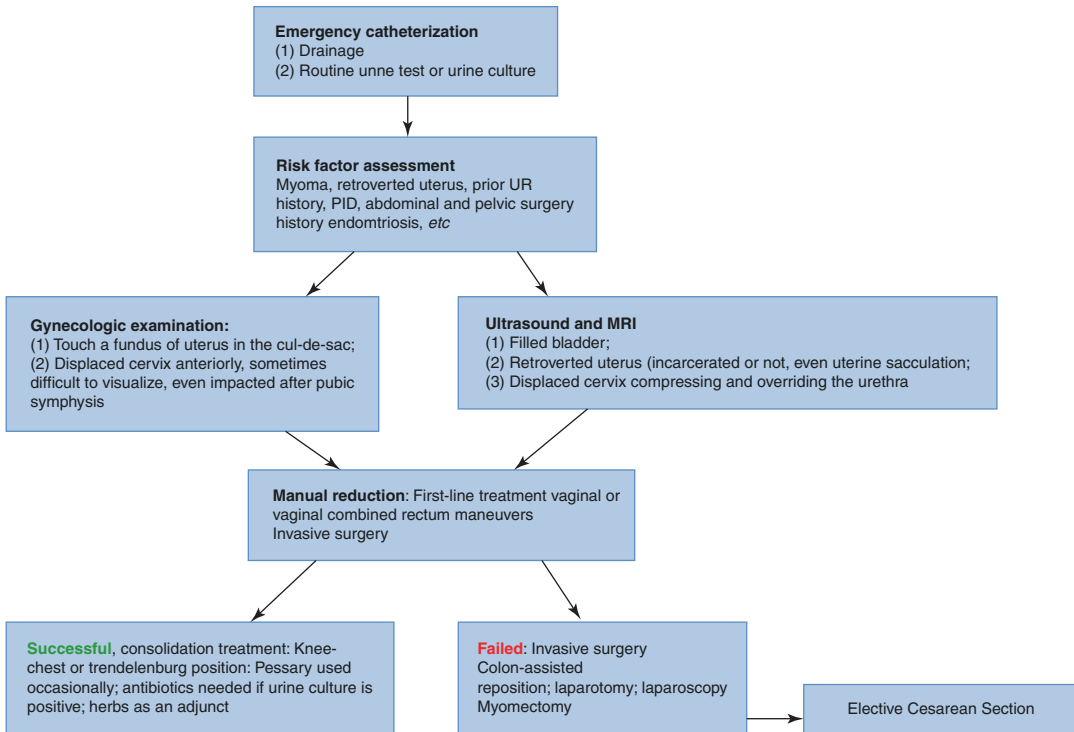
## 28.1.8 Treatment

Mechanical (retroverted uterus) and nonmechanical AUR are treated differently. Nonmechanical AUR necessitates the insertion of a Foley urethral catheter. Duration of catheterization (mostly 7–14 days if an isolated treatment method) depends on the postvoid residual bladder volume. Elective CS is mandatory if uterine fibroids are the cause, and these are removed after unsuccessful nonoperative management (see Chap. 18) [25]. Myomectomy can result in significant loss of blood [25]. The treatment algorithm for antenatal AUR is presented in Fig. 28.8.

Foley urethral catheter is removed when postvoid residual bladder volume is  $\leq 150$  ml [30].

Early diagnosis is essential for successful treatment. The uterus reduction is more likely in





**Fig. 28.8** Strategies for managing acute urinary retention during the first- and second-trimester pregnancy. *MRI* magnetic resonance imaging, *PID* pelvic inflammation

disease, *UR* urinary retention. (Modified and reproduced with permission from [17])

early pregnancy. Late complications like bladder atony, postobstructive diuresis, renal failure, and bladder rupture are due to undiagnosed retroverted and incarcerated uterus leading to AUR [15, 47, 52].

Yang and Huang proposed simple preventive measures [24]:

- Restriction of liquid intake in the evening, before going to bed,
- Urination before going to bed and preventive urination during the night,
- Credé's maneuver, consisting of leaning forward in a sitting position at the beginning of urination,
- Moving from a supine to a prone position before getting up,
- Avoidance of the Valsalva maneuver.

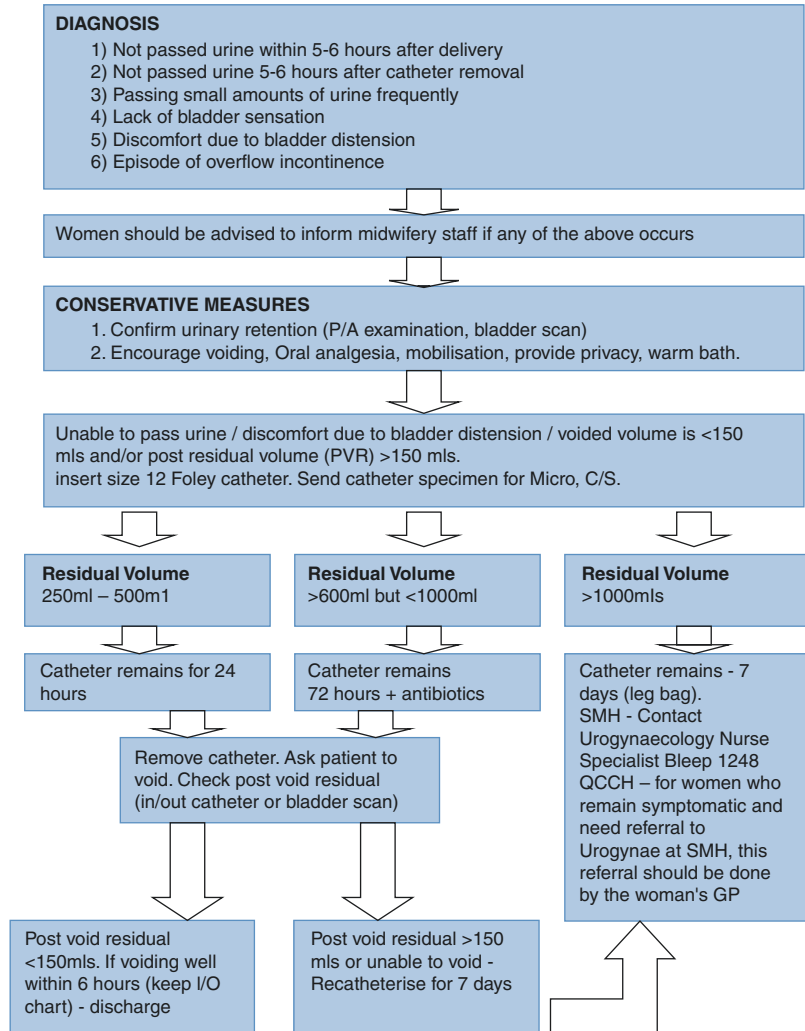
The treatment algorithm for postpartum AUR is presented in Fig. 28.9.

### 28.1.8.1 Manual Reduction

Empty bladder (use a urinary catheter if necessary) and bowel are necessary before the procedure [53]. If the procedure is performed on the awake patient, the patient is given 10 mg of morphine sulfate im. and placed in the knee-chest position. The incarcerated uterus is gently reduced (see next paragraph). In the awake patient, the maneuver of manual uterine reduction results in immediate relief of the tenesmus and bladder discomfort. Postobstructive diuresis may occur following the reduction of the incarcerated gravid uterus [52].

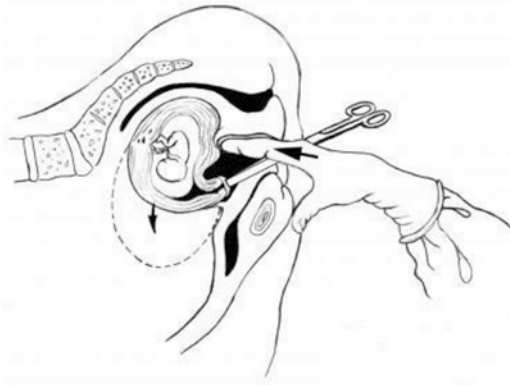
If this fails, frequent knee-chest exercises and daily attempts of manual reduction are performed.

**Fig. 28.9** Imperial college healthcare college healthcare protocol for postpartum acute urinary retention. (Reproduced with permission from [32])



If these fail, general (mostly in advanced pregnancy) endotracheal anesthesia with Propofol induction and succinylcholine for maximum uterine and patient relaxation is done [53]. It is advisable to perform this maneuver under sonographic guidance [53, 54]. Two fingers are placed in the vagina in the posterior fornix. With gentle pressure cephalad on the uterine fundus during the US, the fetal head is displaced from under the symphysis cephalic to the pelvic brim. Gentle and slow pressure prevents separation of the placenta or rupture of the membranes or uterus [12]. US assesses the position of the fetus

and confirms the uterine fundal release. Repeated vaginal examination confirms the absence of the previously palpated uterine mass. Continued pressure applied by the vaginal hand and one hand placed on the abdomen over the fetal head guides the fetus into a cephalic presentation. Gentle but continuous cervical traction can be applied (Fig. 28.10). US reveals the location of the placenta, the cervix, and the fundus in their normal positions. The Foley urethral catheter is left in place, and the patient is on bed rest for 24 h. The final US is done before hospital discharge.

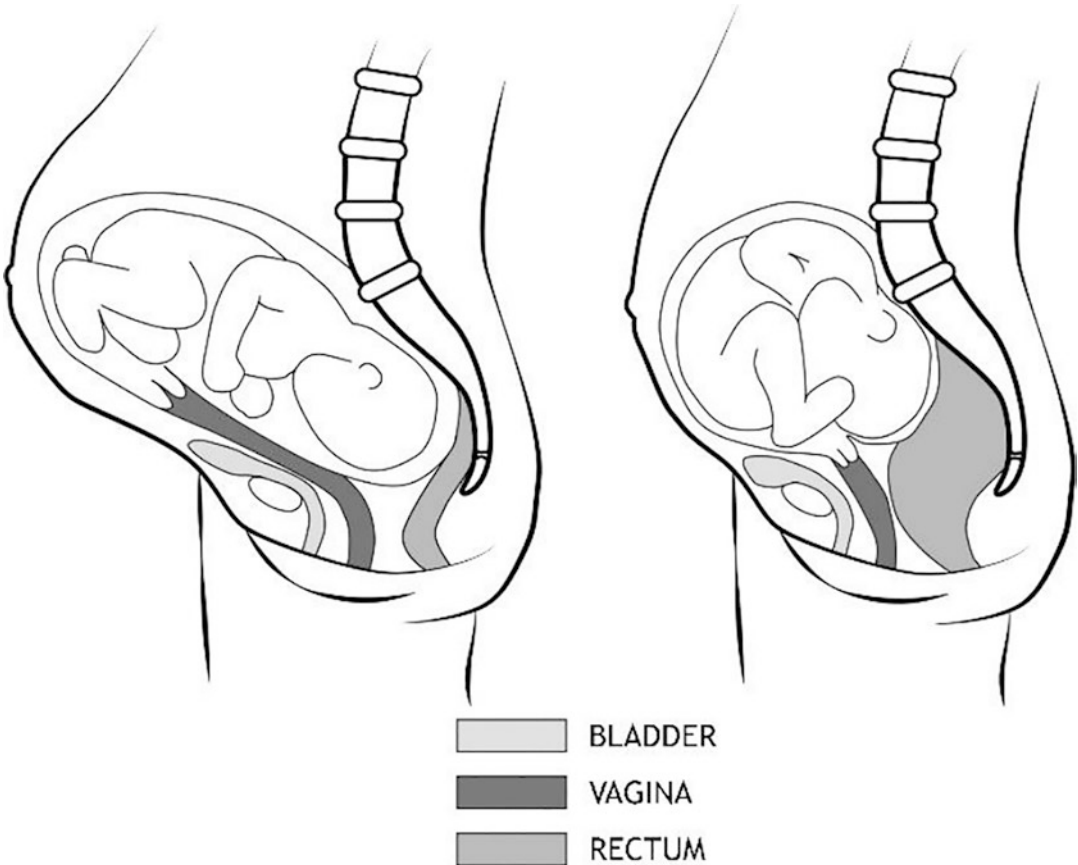


**Fig. 28.10** The technique of manual uterine replacement with the patient in the knee-chest position. (Reproduced with permission from [55])

### 28.1.8.2 Colonoscopic Reduction

If manual reduction fails, sigmoid colon colonoscopic insufflation facilitates manual repositioning of the uterus [41]. A loop is formed when advancing the endoscope through the sigmoid colon [41]. The air insufflation during the procedure and the loop formation have a synergistic effect by creating anterior pressure through the rectum wall on the uterine fundus (Fig. 28.11). The ability of the colonoscope to create an air cushion underneath the incarcerated uterus makes the success rate of this procedure higher than that of manual maneuvers.

Once reduced, a uterus large enough to become impacted usually will remain an abdomi-



**Fig. 28.11** Colonoscopy-assisted repositioning of the incarcerated uterus. The ability of the colonoscope to get above the uterine fundus, together with the extra anterior

pressure provided by the loop formation and air insufflation, makes the success rate higher than the manual maneuvers. (Reproduced with permission from [56])

nal organ with no additional support, though a pessary may be needed occasionally. The pessary can be removed once the ascent of the gravid uterus is documented by physical examination after the first trimester.

### 28.1.8.3 Surgical Reduction

Unsuccessful conservative reduction of 3–4 days indicates operative reduction [57], with [58] or without placement of the pessary. More invasive treatment modalities like reduction with laparoscopy or laparotomy carry the risk of maternal and fetal morbidities [27, 59].

### 28.1.8.4 Obstetric Management

Increased bleeding is expected due to easier passage of uterine contents after manual reduction of the incarcerated uterus [57]. Bleeding mandates subsequent suction and curettage [57].

### Prevention and Treatment of Preterm Labor

See Chap. 4.

## 28.1.9 Prognosis

AUR due to the retroverted gravid uterus is a risk factor for AUR recurrence during the next pregnancies [24, 43] and even in the same pregnancy [43].

The possibility of recurrence of AUR should be explained to patients with the necessity of preventive measures to minimize the possibility of AUR during the first trimester of their subsequent pregnancies (see Sect. 28.1.7). The reasons for recurrence are unclear because there are no other abnormalities except for retroversion of the uterus contributing to AUR [24, 43]. Few women reported any issues with voiding up to 4 years after their episode of antenatal AUR; in those that did, they were an occasional occurrence. Therefore, there is little impact on quality of life, bowel, or sexual function [21].

Although postpartum AUR may be a transient phenomenon [60], a single episode of bladder distention can irreversibly damage the detrusor muscle, resulting in permanent voiding dysfunction [8]. Furthermore, preexisting voiding dysfunction, renal disease, or acute urinary tract infection influence prognosis. In contrast to intrapartum AUR, the clinical course of postpartum AUR is longer. It implies a longer need for catheterization, which indicates that the damage to the bladder is more severe. Approximately 45% of women with overt postpartum AUR resolve within 48 h, 30% by 72 h, and 25% continued to have retention for >72 h. Finally, all women have a resolution of symptoms [61]. Patients with postvoid residual bladder volume <750 ml require a significantly shorter duration of bladder catheterization (17 days) compared to those with >750 ml (27 days) [62]. In postpartum settings, postvoid residual bladder volume ranges from 600 to >2000 ml [8, 11]. Despite all this, postpartum AUR has no long-term effects on pelvic floor dysfunction [21].

No treatment or a delay of AUR treatment, especially during labor, increases the risk of urinary bladder rupture (see Sect. 28.3). Intermittent or short-term urethral catheterization does not increase the risk of urinary tract infection.

## 28.2 Renal Collecting System or Parenchymal Rupture

### 28.2.1 Incidence and Etiopathogenesis

In pregnancy, renal pelvis rupture involves 1.9% of all cases [63].

The mechanisms of spontaneous renal rupture in pregnancy are [64]:

- True spontaneous rupture (with no cause),
- Rupture of the excretory tract related to an obstruction,
- Renal rupture secondary to kidney pathology.

#### 28.2.1.1 True Spontaneous Rupture

Hydronephrosis may develop from the sixth to the tenth week of gestation [65] and is symp-

tomatic in 3% [66]. According to Gillenwater, a rupture of the collecting system can occur from week 18 of gestation to day 1 postdelivery [67]. To result in a rupture, the hydrostatic pressure must exceed the holding capacity of the calyceal-renal capsular junction [67] and the protective mechanism of spontaneous extravasation of the urine through the calyceal fornices. The increased pressure within the pelvicalyceal system generates stretching and decreases the elasticity of the capsule and soft tissue attenuation [65]. It is surmised that forniceal rupture is a safety valve to alleviate increased intrapelvic pressure. According to Laplace's law ( $\text{Tension} = \text{Pressure} \times \text{Radius}$ ), the tensile stress that accumulates within a dilated collecting system would increase with size, causing an earlier forniceal rupture in a more dilated system [63]. A pressure that exceeds the tensile strength of forniceal tissues leads to rupture and extravasation of urine. This may occur when renal pelvis pressure exceeds a critical level between 70 and 75 mmHg [68]. A higher probability of a rupture is in areas where a normal structure is altered by infections, tumors, or scarring [69].

A sudden increase in intrapelvic pressure may result in spontaneous extravasation of urine through the calyceal fornices. This physiological protective phenomenon will result in pyelotubular, pyelosinus, and pyelolymphatic backflow. This extravasation resolves spontaneously and without sequelae [70]. A true rupture of the renal pelvis is quite different and results in urine extravasation into retroperitoneal space. Urine and blood can dissect along fascial planes to produce an extensive retroperitoneal urinoma, hematoma, or later abscess or perirenal pseudocyst. These dissections may break through the peritoneal covering and produce chemical or infective peritonitis.

Colin Campbell (Manchester, UK) described the first spontaneous calyceal rupture without underlying disease in 1947 [71]. Between 1947 and 1995, 25 cases were published—12 with ruptures of the collecting system and 13 with ruptures of the renal parenchyma [72]. In 2010, 18 cases of spontaneous renal rupture during pregnancy were collected, 13 in patients with normal kidneys. Up to 2015, 37 spontaneous urinary tract rupture cases during pregnancy were

published; left to right ratio = 1 : 3 [73, 74]. Spontaneous ruptures without obstruction in the nonpregnant state are predominantly right-sided (13/16). Explanations for right-sided predilection are [75, 76]:

- The hormonal ureteral atony,
- Compression of the right ureter caused by the physiological dextrorotation of the gravid uterus,
- Engorged right ovarian artery or vein.

### 28.2.1.2 Upper Urinary Tract Obstruction

Most nontraumatic pelvic or calyceal ruptures in a normal kidney result from compression [77]. The increase in size and changes in the parenchyma structure make the lesions more susceptible to minor trauma from external or internal sources [78].

The pregnancy-related obstruction can be due to [79]:

- Incarcerated gravid uterus,
- Chronic ectopic pregnancy,
- Polyhydramnios,
- Normal pregnancy.

Although calyceal rupture can occur in kidneys without preexisting pathology, many spontaneous upper urinary tract or kidney ruptures during pregnancy are associated with renal calculi [73, 80]. There are only two cases of rupture from renal pelvis calculi [81, 82] and one from distal ureteral stone [83].

### 28.2.1.3 Renal Parenchymal Rupture

The neoplasms are the most common cause, and renal angiomyolipoma (see Sect. 29.3) is the most frequent among neoplastic causes.

### 28.2.1.4 Other

After urinary tract calculi, previous urinary tract infection is the most commonly encountered in patients with renal fornix rupture [84]. More than half had some form of underlying kidney pathology, such as infection, abscess, stones, or tumors, either in the past or during rupture [73, 74].



28.2.2 Clinical Presentation

28.2.2.1 Medical History

The initial manifestations of pyeloureteral leakage range from mild flank discomfort to unremitting pain associated with peritonism from rupture. With spontaneous renal forniceal rupture (SRFR), the pain preceded the clinical presentation from 1 day to 6 weeks [84]. The right side was most frequently affected (67%), with 5% complaining of bilateral discomfort [84]. Pain is due to urine or blood dissecting along the fascial planes with or without disrupting the peritoneal covering to produce infective or chemical peritonitis [78]. Sometimes the pain may be associated with pyrexia, suggesting an infected urinoma, abscess, or chemical peritonitis. Suprapubic pain suggests the level of obstruction or infection.

Additionally, the patient can present with nausea and vomiting. A history of a remote UTI or urolithiasis before the current pregnancy can be elicited [74]. Anuria can be present with complete obstruction of the ureters by the gravid uterus [79]. A renal abscess is probable if fever is present with flank pain and a palpable mass [64].

28.2.2.2 Physical Examination

Signs depend on the cause of the rupture and the level of obstruction if present. Palpable mass in the lumbar region is common with (ruptured) renal angiomyolipoma (RAML) [85]. Percussion flank tenderness is common. The obstruction at the level of the vesicoureteric junction or distally results in abdominal or suprapubic tenderness. Peritoneal signs are mostly absent. This presentation may be associated with pyrexia, suggesting an infected urinoma, abscess, or chemical peritonitis. Mild tachycardia is common [73]. A palpable mass made of urinoma and blood can be felt with a parenchymal tear on examination of the flank [65].

Parenchymal renal ruptures are associated with sudden hematuria, loin pain, loin mass, or hypotension, while a calyceal rupture usually presents with loin pain with or without hematuria [72] but without hypotension.

**Table 28.2** Differential diagnosis of flank pain in pregnancy [74, 86, 87]

|                                  |                                     |
|----------------------------------|-------------------------------------|
| No blood loss                    | Blood loss                          |
| Acute hydronephrosis             | Spontaneous renal rupture           |
| Nephrolithiasis/<br>urolithiasis | Spontaneous liver/spleen<br>rupture |
| Acute pyelonephritis             | Heterotopic/ectopic<br>pregnancy    |
| Renal cysts                      | Spontaneous uterine rupture         |
| Renal malignancy                 | Placental abruption                 |
| Constipation                     | Renal angiomyolipoma                |
| Gastrointestinal<br>infections   | Renal artery aneurysm<br>rupture    |
| Acute appendicitis               |                                     |
| Acute cholecystitis              |                                     |
| Acute pancreatitis               |                                     |
| Ovarian cysts/tumors             |                                     |
| Uterine fibroids                 |                                     |
| Pelvic inflammatory<br>disease   |                                     |
| Musculoskeletal pain/<br>trauma  |                                     |
| Cystitis                         |                                     |

28.2.3 Differential Diagnosis

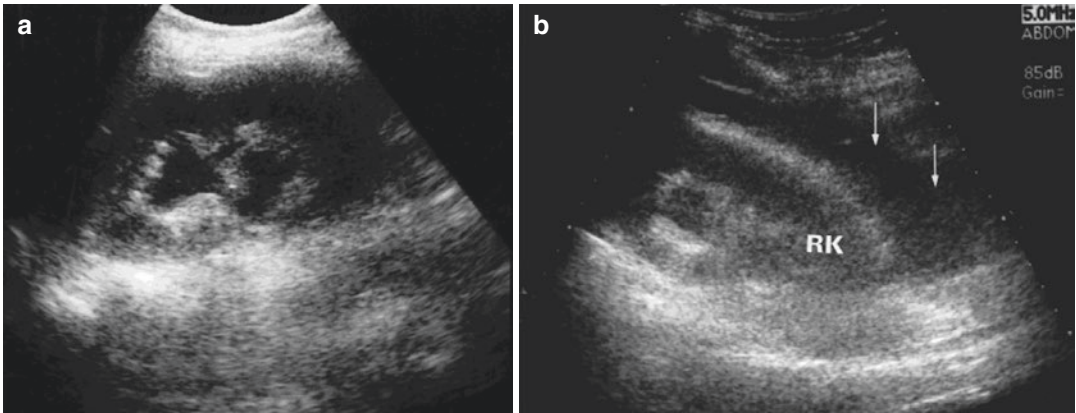
Renal rupture during pregnancy with a nonspecific abdominal complaint can be confused with other causes of acute abdomen. Flank pain during pregnancy is a common complaint with a broad differential diagnosis (Table 28.2). Appendectomy was performed inappropriately in 17% of patients with SRFR [84]. With hematuria, the diagnoses are mostly urologic.

28.2.4 Diagnosis

The diagnosis of spontaneous renal rupture during pregnancy is often one of exclusion.

28.2.4.1 Laboratory Findings

Laboratory testing is usually not diagnostic, although normal serum liver function tests, amylase, and lipase levels rule out the liver, biliary, and pancreatic pathologies. Leukocytosis is present in 50% with SRFR [84]. BUN and creatinine levels depend on the preexisting renal status and the cause of renal/collecting system rupture. BUN and creatinine levels are elevated with obstruction, with SRFR in 19% [84].



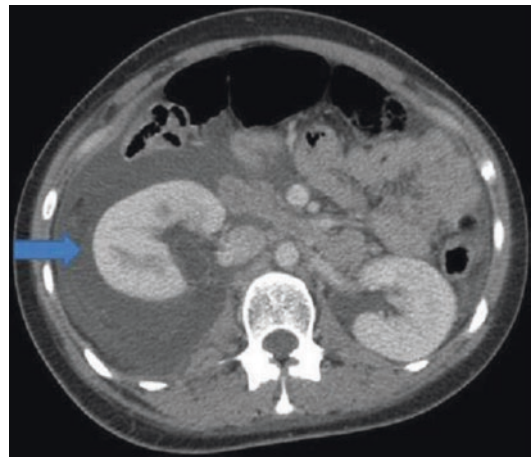
**Fig. 28.12** Hydronephrosis resulting in a renal rupture in a primipara with right flank and right lower quadrant pain at 28 weeks of pregnancy. (a) Sonogram on admission shows diffuse enlargement of the right kidney with moderate hydronephrosis. (b) Follow-up sonogram for persistent

right flank pain 3 days after an appendectomy reveals a small amount of anechoic fluid (white arrows) in the inferior aspect of the right perinephric space. RK, inferior pole of the right kidney. (Reproduced with permission from [88])

Urinalysis can reveal UTI or more pronounced bleeding due to urinary tract calculi, while urine culture sometimes does not confirm bacterial growth [74]. Spontaneous renal fornix rupture results in hematuria in 36%, leukocyturia in 31%, and positive urine culture in 27% [84]. Nitrites and leukocytes in the urine are indicative of UTI [73]. Macro- or microhematuria is more common with parenchymal rupture than with rupture of the collecting system [77].

#### 28.2.4.2 Transabdominal Ultrasound

Doppler US detects ruptured kidneys and hydronephrosis [88]. Serial US is indicated, especially for symptomatic patients with minimal benign-appearing perinephric collection on initial US [65]. The differentiation between physiological and pathological dilatation of the renal collecting system in pregnant patients is based on the extension of the dilated ureter over the common iliac artery. Physiological hydronephrosis will extend down only to the level of the artery. In contrast, in a pathologic obstruction, it will extend below the artery [89]. SRFR can be visualized as ureteral calculi or perinephric collection without the cause of obstruction (Fig. 28.12). The US has limitations in detecting or locating small ruptures. Its accuracy for urinary extravasation from SRFR is 52% [84]. Maresca et al. made the first US diagnosis of SRFR in 1981 [87].



**Fig. 28.13** Native abdominal CT without nephrolithiasis reveals urinoma (blue arrow). (Reproduced with permission from [91] under the CC Attribution License)

Serial transabdominal US evaluates residual collections every 2–4 weeks after radiologic or surgical interventions [90].

#### 28.2.4.3 Abdominal CT

Computed tomography (CT) is the modality of choice for postpartum presentation (88%) [84]. Native abdominal CT defines urinoma, differentiating it from hematoma according to the Hounsfield units (Fig. 28.13).

**28.2.4.4 Abdominal MR/MR Urography**

With uncertain US findings and hemodynamically stable patients, abdominal MR is recommended. Its use increases from 11% before 2015 to 67% between 2015 and 2020 [84]. The evolution of diagnostic imaging modalities through decades is presented in Fig. 28.14.

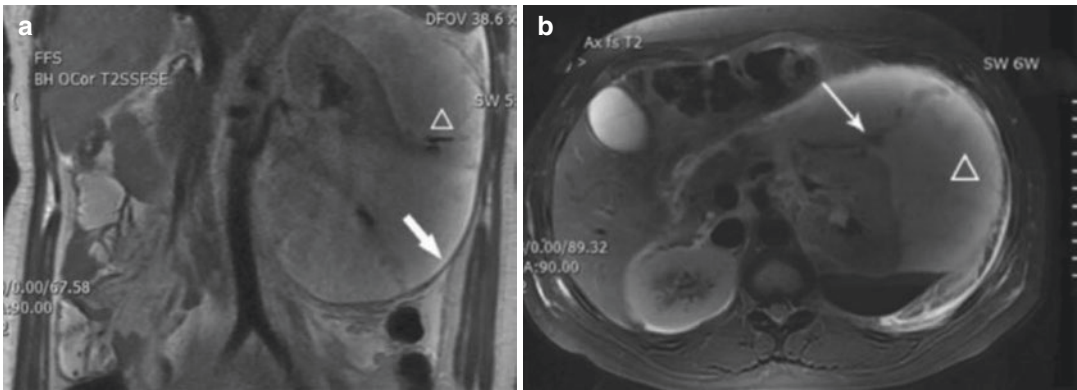
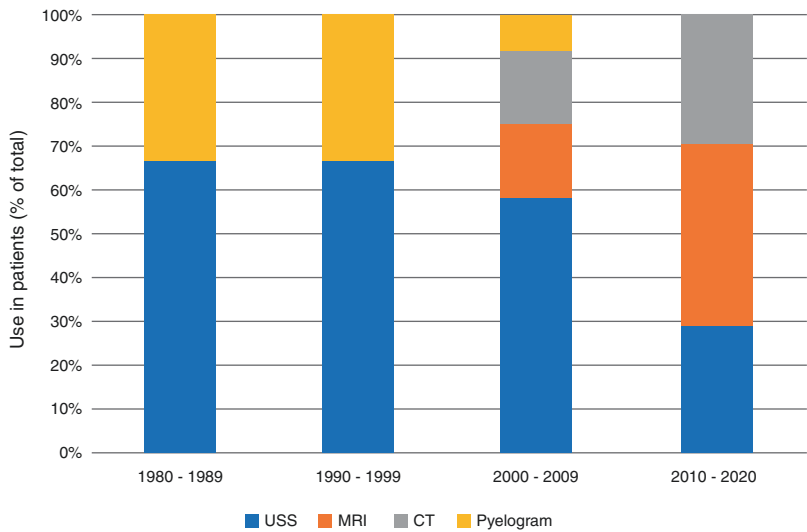
MR can delineate perinephric fluid (Fig. 28.15) and retroperitoneal fluid consistent with calyceal rupture and urine leak (Fig. 28.16). Urinary tract stones are usually detected [74]. The MR replaced

excretory urography due to its ionizing radiation. It distinguishes urinoma from hematoma by the characteristic high-intensity signals of the acute hematoma on the T1-weighted images [88].

**28.2.4.5 Excretory Urography**

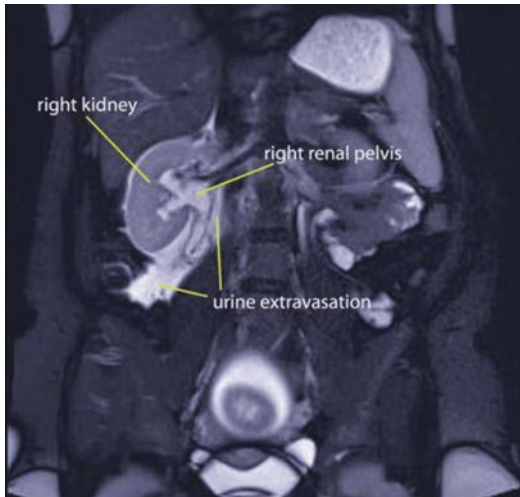
Before the widespread use of abdominal CT and MRI, excretory urography defined urinary tract pathologies. IV urogram with two films (<1 rad) can identify the rupture site without associated harm to the fetus [92]. Dilation of the urinary tract system or extraluminal contrast was

**Fig. 28.14** Distribution of diagnostic imaging modalities used to diagnose spontaneous renal forniceal rupture during the last four decades. (Reproduced with permission from [84] under the CC Attribution License)



**Fig. 28.15** (a) MRI coronal view shows the fluid (Δ) localized under the left renal capsule (→). (b) MRI axial view shows the rupture of the left kidney (→) and the fluid

extravasation around it (Δ). (Reproduced with permission from [90] under the CC Attribution License)



**Fig. 28.16** MRI shows right renal pelvis rupture without distal calculi. (Reproduced with permission from [75])



**Fig. 28.17** Limited excretory urogram at 34 weeks of pregnancy shows extravasation of contrast in the lower pole of the right kidney (arrow). The fetal skeleton is visible. (Reproduced with permission from [78])

diagnostic (Fig. 28.17). Urinary tract calculi were visualized depending on the radiolucency. It showed the site and the nature of the rupture or obstruction, the amount of extravasation, and the function of the kidneys (Fig. 28.18).

## 28.2.5 Treatment

No consensus or evidence-based options exist for treating spontaneous urinary tract rupture in pregnancy. The management depends on the underlying cause, a rupture site and a degree [80], fetal status, and maternal hemodynamic stability. The treatment goals are to preserve renal function, relieve pain, allow the rupture site to heal spontaneously [93], and promote the safe progress of the pregnancy to term and safe delivery with minimal disturbance for the baby [73].

### 28.2.5.1 Conservative Treatment

There is no indication for surgical intervention with clinical improvement after renal collecting system rupture. Conservative management may be applied to small perinephric collections [65]. Analgesia should be titrated. Leukocyte, BUN, creatinine levels, and urinalysis are regularly checked to detect disease progression. Antibiotics are administered if urinalysis or urine culture is positive. Conservative treatment was completed in 15% for spontaneous renal fornix rupture, commonly used in patients reaching term delivery [84].

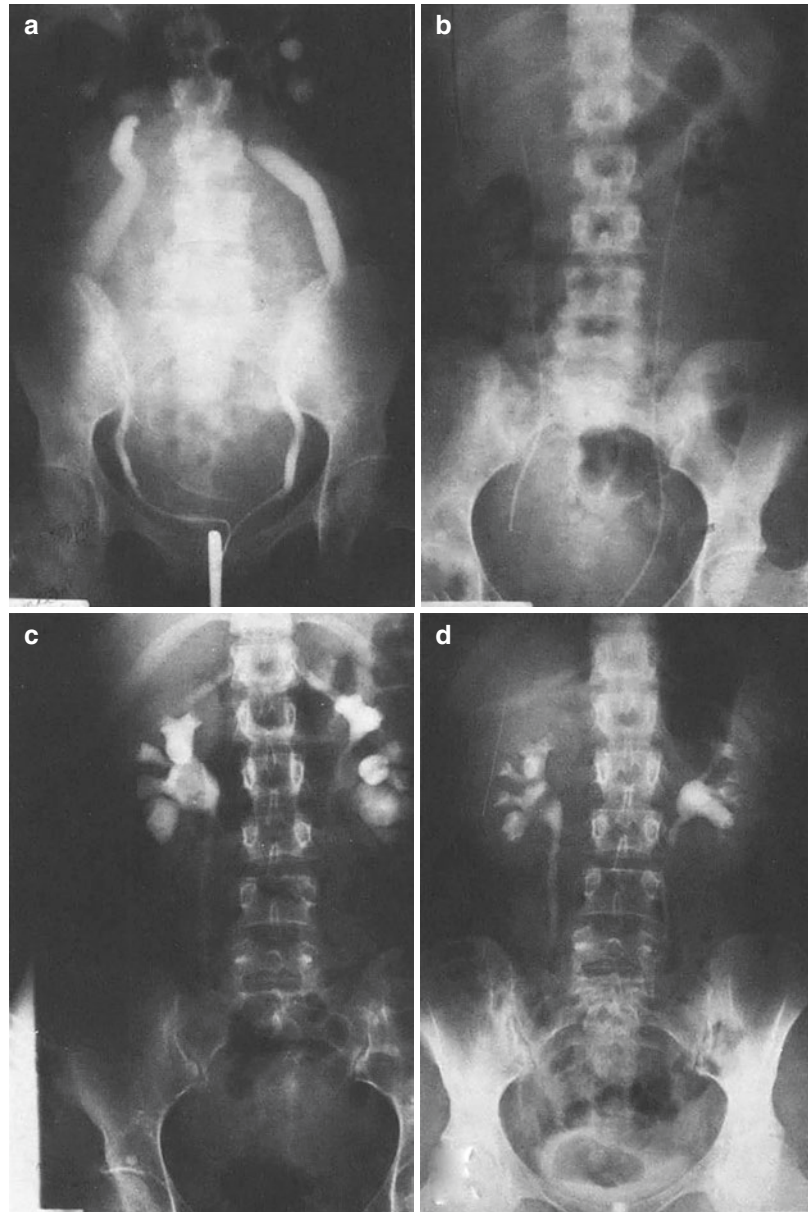
Hydronephrosis of pregnancy is mostly benign, and relief of renal colic from acute obstruction may be obtained by a positional change to the left lateral or knee-chest position [94]. Retroverted or incarcerated uterus rarely causes upper urinary tract obstruction but bladder obstruction (see Sect. 28.3.5). Evens spontaneous or induced (pre)term labor eliminates or minimizes both symptoms and the need for further treatment [74].

### 28.2.5.2 Interventional Techniques

A JJ stent is probably the least invasive, effective method for controlling pain and progression of the rupture and allowing the pregnancy to progress to term. The advantages of a JJ stent are pain relief and free drainage, facilitating the closure of the communication between the pelvicalyceal system and perinephric space [65]. Stents are also indicated when gravid uterus compression causes severe bilateral hydronephrosis (Fig. 28.18). Obstructive cause,



**Fig. 28.18** (a) Initial placement of ureteral catheters under local anesthesia, (b) ureteral stents in place. IV urograms, (c) a day after stent removal and 3 weeks after full-teen delivery, and (d) 8 weeks after stent removal. (Reproduced with permission from [79])



such as a persistent large renal stone following calyceal rupture, mandates more aggressive intervention, such as ureteroscopic lithotripsy combined with ureteral stenting. Appropriate FDA class B antibiotics and close follow-up are essential.

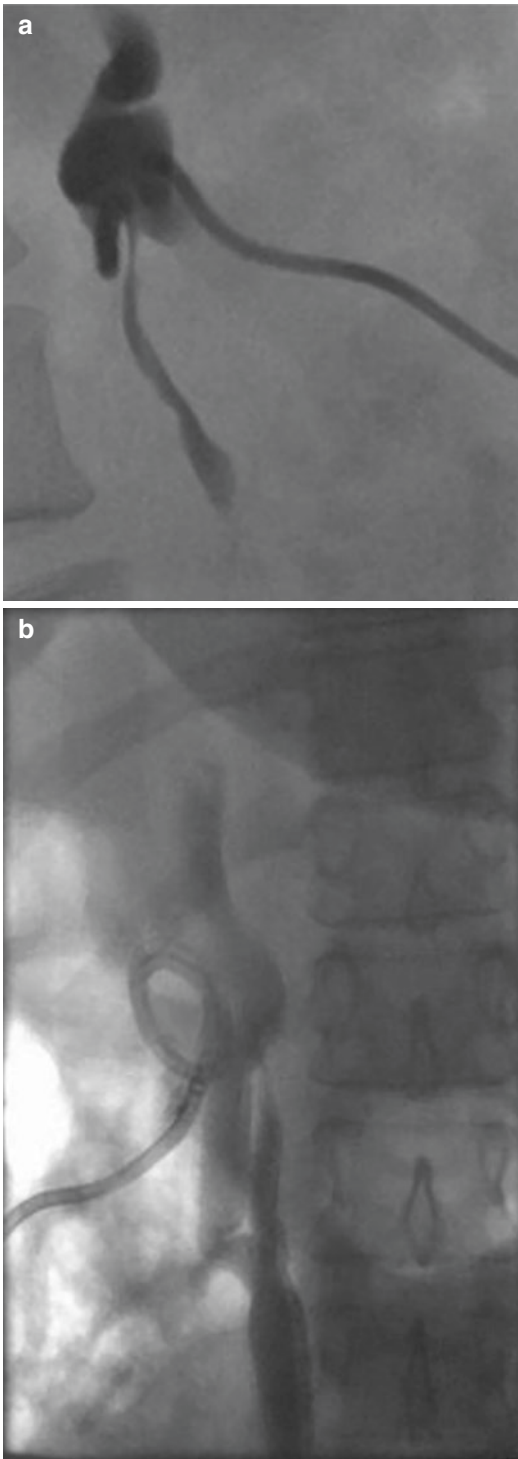
For SRFR, all stents were removed between 2 and 8 weeks postpartum (mean: 4 weeks), with a mean in situ time of 8.8 weeks (range 2–21 weeks) [84].

### 28.2.5.3 Surgical Treatment

#### Percutaneous Nephrostomy

While analgesia and conservative therapy are appropriate forms of initial management for patients with symptomatic obstruction. Persistent pain [80, 95] or enlarging urinoma [90] mandates percutaneous nephrostomy or ureteral stenting. Percutaneous nephrostomy (Fig. 28.19) is indicated when retrograde ureteric stenting fails because of the tortuosity





**Fig. 28.19** (a) Placement of ureteral catheters and (b) catheter in place during remaining pregnancy. (Reproduced with permission from [73] under the CC Attribution License)

of the dilated ureter [80]. The tube insertion into the urinoma provides better and faster fluid drainage and reduces pressure on the kidney compared to JJ stents. A nephrostomy tube is removed when there is no further drainage. Sometimes, after (induced) labor, symptoms resolve spontaneously without surgical intervention [74]. Nephrostomy was performed in 13% of SRFR [84].

During CS, sample of the retroperitoneal fluid is diagnostic. It can reveal hematoma; if yellow, creatinine levels should be compared with urine creatinine levels [90].

### Exploration

Exploration is indicated when (bilateral) ureteral obstruction cannot be relieved, and the compressing mass should be removed [96].

#### 28.2.5.4 Obstetric Management

Ureteral obstruction secondary to compression by the massively enlarged uterus with polyhydramnios results in renal failure. Attempts at amniocentesis are usually unsuccessful. Therefore, the induction of labor by amniotomy is the treatment of choice [97].

Maternal hemodynamic instability due to the ruptured RAML increases the rate of emergent CS by 50%. Term vaginal delivery after antepartum-ruptured RAML with hemodynamic stability is successful under strict monitoring of maternal and fetal status [98]. There is no evidence that the incidence of RAML rupture during vaginal delivery is higher than during CS.

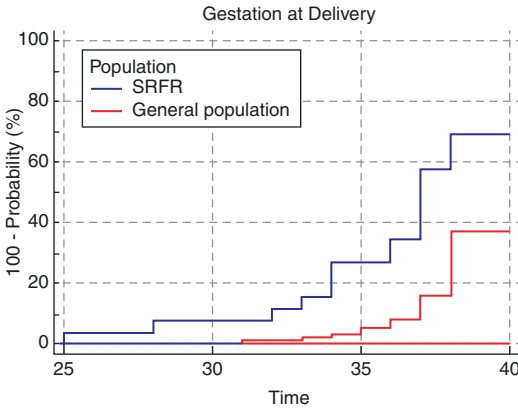
### Prevention and Treatment of Preterm Labor

See Chap. 4.

#### 28.2.6 Prognosis

##### 28.2.6.1 Maternal Outcome

The natural course of renal collecting system rupture is the resolution of symptoms following rupture if no secondary infection develops. No guidelines exist regarding puerperal management and how to counsel patients in subsequent pregnancies.



**Fig. 28.20** Comparative Kaplan-Meier probability of delivery according to gestation between the general pregnant population and pregnant patients with SRFR. *SRFR*, spontaneous renal fornical rupture. (Reproduced with permission from [84] under the CC Attribution License)

Maternal mortality is 0% [84]. Overall, no significant long-term urologic complications were reported after SRFR, with all patients responding well to treatment [84]. Pregnancy complications were more common, with an average gestational week at delivery of 36.3. Preterm delivery occurred in 34% (Fig. 28.20). Two-thirds of the patients had a (instrumental) vaginal delivery (69%), while the remaining underwent CS [84].

Renal failure caused by obstruction does not occur in pregnant patients with ectopic or pelvic kidneys, although an increased rate of CS is due to difficult labor.

#### 28.2.6.2 Fetal Outcome

Fetal outcomes may be adversely affected by the increased rate of premature delivery. Fetal mortality after SRFR is almost 0%. A single neonatal death occurred, most likely due to extreme prematurity following a 26-week delivery in a case of suspected cervical incompetence [84].

## 28.3 Urinary Bladder Injury or Rupture

Urinary bladder injury or rupture is rare in pregnancy and puerperium. Current guidelines and consensus statements of the *European*

*Association of Urology* [99] and *Société Internationale d'Urologie* [100] do not discuss pregnancy-associated bladder injuries.

### 28.3.1 Incidence

The incidence of bladder injury during CS ranges from 0.0016 to 0.94% [101–105], increasing with previous abdominal surgery, previous CS, the prolonged second stage of labor, or Cesarean hysterectomy [102]. The incidence is unchanged during the last half of the century. The dome of the bladder is most frequently injured [106]. The incidence of simultaneous uterine and bladder rupture is 1/32–1/251 [107, 108] of uterine ruptures, although a significantly higher association has been reported [109].

### 28.3.2 Etiopathogenesis

#### 28.3.2.1 Spontaneous Bladder Rupture

##### Underlying Pathology

In the general population, spontaneous bladder rupture is associated with trauma, malignancies, anatomical outflow obstructions, indwelling catheters, instrumentation, neurogenic bladder, or a combination [110]. Rare cases of bladder rupture during pregnancy are associated with underlying diseases, such as necrotizing cystitis [111], bladder diverticulum [111], bladder tumor [112], (prolonged) vaginal labor [113, 114], a trial of labor following CS or gravid uterus prolapse/displacement [115, 116].

##### Pregnancy, Delivery, and Puerperium

The bladder rupture during pregnancy primarily results from obstruction. Retroversion is normal in up to 20% of healthy women. By 14–15 weeks, as the uterus enlarges, it grows out of the bony pelvis like an anteverted uterus. It is possible that the uterus is impacted for a few days causing voiding difficulties and later retention with overflow [117]. The retroverted incarcerated uterus is a major risk factor for bladder rupture empha-

sized by Torpin in 1940 [118], later by Sarkar in 1944 [116], and Mussgnug in 1947 [119], resulting from prolonged urinary bladder obstruction.

In 1940, Torpin realized that delivery and early puerperium are the most frequent gestational periods for bladder rupture [118]. Intraperitoneal urinary bladder rupture following vaginal delivery is isolated or combined with uterine rupture [120], mostly after previous CS [121, 122]. Isolated extraperitoneal bladder rupture following vaginal delivery is extremely rare [123, 124]. Intrapartum and postpartum states lead to poor bladder emptying, increasing the tendency for AUR following delivery. Epidural anesthesia increases the risk of AUR (see Sect. 28.1.3.2) and probably increases the risk for urinary bladder rupture.

The fetal head compresses the distended urinary bladder over the pelvic brim and symphysis pubis during forceful uterine contractions, leading to pressure necrosis of the bladder dome during delivery or early puerperium [125]. Bladder rupture during puerperium can occur due to its incomplete evacuation from pain or primary bladder pathology. Thus, adequate postdelivery bladder evacuation prevents this complication. Without catheterization, bladder rupture is more likely during labor. Postpartum patients undergoing episiotomy or perineal repair frequently experience voiding difficulties, leading to AUR. Interestingly, as these patients frequently pass a small amount of urine, AUR may go unnoticed. The retention may result in gross bladder distention and subsequent spontaneous rupture [126]. Without bladder wall pathology, the weakest part is usually the dome of the bladder [125].

All women should be catheterized if they have not voided within 6 h after vaginal or CS to decrease complications associated with postpartum AUR [127].

Bladder rupture is preventable if the bladder is empty during the second stage of labor. Also, early ambulation helps in emptying the bladder.

### Uterovesical Rupture

The urinary bladder involvement in uterine rupture is distinctly rare in the absence of adhesions of the urinary bladder to the lower uterine segment; hence, rare in the unscarred uterus [128] and distinctly unusual in a primigravida when prolonged labor is a risk factor [107]. Therefore, it is most common following a (trial of) vaginal delivery after a previous CS [120].

The bladder should always be inspected in an anterior rupture of the lower segment.

Contrary to spontaneous isolated bladder ruptures (bladder dome ruptures), uterovesical ruptures result in large posterior rents in the bladder, frequently involving the cervix and vagina [120]. The trauma mainly involves the area around the bladder base and the ureteral orifices [120]. The appearance of the ruptured uterus and bladder with exposure to the trigone is most alarming. The lower edges of the bladder tears retract posterolaterally and bleed. Friability of the edges, the proximity of the ureters, and bleeding all cause difficulty. The muscular cervix behind provides a firm buttress for the sutured organ. The instances of the above severe and unusual obstetrical injury urge us to consider the anatomical relationship between the uterus and bladder and the technique of the lower-segment CS. Caudalwards to the uterovesical fold of the peritoneum, the lower part of the anterior wall of the uterus, and the upper portion of the vagina are in close contact with the posterior wall of the bladder. The interposition in this potential space of loose cellular tissue always permits limited bladder movement and expansion of the uterus in pregnancy. The visceral pelvic fascia is reflected upwards for a short distance onto the posterior wall of the bladder and the anterior wall of the uterus. It becomes fused to their connective tissue coats, on which the vesical and uterine vessels and nerves form dense plexuses. Then, interposed between the bladder and uterus are connective tissue, blood vessels, lymphatics, and nerves.

Observation of the bladder, at different stages of filling, during abdominal operation shows that the fundal portion and the anterior wall undergo active distension, the lower posterior wall remaining relatively immobile. Free movement of the bladder on the uterus is not intended below the uterovesical fold of the peritoneum. The loose cellular tissue comprises fine connective fibrils with abundant but poorly supported blood vessels. After surgical trauma, a clot results in scar tissue, denser and coarser than the cellular tissue in which it develops. Scarring is more pronounced with infection, edema, exudation, and fine fibrosis. When, after CS, the posterior wall of the bladder becomes adherent to the transverse incision in the lower segment of the uterus, coincidental violent rupture of both organs is likely to occur if splitting or tearing should begin in the uterine scar in a subsequent pregnancy or labor.

28.3.2.2 Urinary Bladder Injury

Cesarean Section

CS increases the risk of urinary bladder injury due to its proximity. Prior CS is a significant risk factor for bladder injury occurring at the time of a CS, conferring a 4–5-fold increased risk over a primary CS [102, 105]. In other words, prior CS accounts for 67–72% of bladder injuries [102, 105]. In particular, adhesion formation between the bladder and lower uterine segment is likely to be a causative factor because 34.2% of bladder injuries occurred during the formation of the bladder flap [102, 105]. A large baby (fetal weight >4000 g) was found to be an independent risk factor for bladder injury [105]. This may cause uterine wound extension with an injury to the bladder. The presence of labor is an independent risk factor for bladder injury during CS [102, 105]. Moreover, the presenting fetal part station greater (deeper) or equal to +1 was an independent risk factor for bladder injury, with an OR of 2.4 [105]. Emergency CS is another significant risk factor for bladder injury, especially in patients with previous CS [102, 129]. A complete list of factors that increase the risk of bladder injury during CS is in Table 28.3.

**Table 28.3** Conditions associated with bladder injury during Cesarean section [130, 131]

|                                                                     |
|---------------------------------------------------------------------|
| Prolonged labor with a distended bladder                            |
| Obstructed labor                                                    |
| Postcesarean pregnancy                                              |
| Postmyomectomy pregnancy                                            |
| Postlaparotomy pregnancy                                            |
| Altered anatomy or fibrosis                                         |
| Direct extension of disease                                         |
| History of uterine perforation, septic abortion                     |
| Presenting fetal part deeper than or equal to +1                    |
| Fetal weight >4000 g                                                |
| Well effacement and dilatation of the cervix                        |
| Preterm Cesarean section where the lower segment is not well-formed |
| Type of Cesarean section                                            |
| Cesarean hysterectomy                                               |
| Ruptured uterus                                                     |
| Placenta percreta penetrating the bladder                           |
| Multiple Cesarean sections                                          |
| Type of placenta                                                    |

As in total hysterectomy, downward dissection of the bladder is unnecessary and inadvisable. It results in fine hemorrhages in the cellular tissue and opens the space for spreading infection if this should occur during the puerperium. In CS, the uterovesical fold of the peritoneum is picked up and divided transversely. With the index finger, the peritoneum and underlying fascia are separated from the uterus immediately below the level of the incision in the peritoneum itself. This exposes the uterine muscle, into which the cesarean incision is made. The upper limit of the bladder, with its venous plexuses, is seen, but its downward displacement, if at all affected, should be limited to the traction force of the bladder retractor. The process, variously described as “wiping-down,” “blunt dissection,” “gauze dissection,” “disengagement,” or “mobilization” of the bladder, should be both gentle and slight.

The transverse incision in the uterus is sufficiently close to the cervix to be a strictly lower segment in position. In labor, the “assumption” of the cervix into the lower segment and the expansion of that part of the uterus render a truly lower-segment section or even a laparotrachelotomy practicable without vigorous bladder displacement [132].

### Total Hysterectomy

The urinary bladder or ureter could be injured during a total hysterectomy [132].

### Blunt Abdominal Trauma

The most common causes of blunt abdominal trauma are motor vehicle accidents, falls, and domestic trauma. Urinary bladder ruptures result from compression on the inferior abdomen [133]. Sudden pressure on the abdominal wall spreads to the bladder, then projects itself on the posterior wall of the pelvis. Due to its resistance, it comes back toward the bladder (anterior), giving it a counterblow. Several conditions may contribute to the extent of the lesions. The amount of urine inside the bladder during injury plays an important part. If the bladder is empty, it can be torn only through the direct impact of the trauma agent on its walls because of its deep location in the pelvis and its protection by pelvic bones. The entire bladder comes out of that protection and becomes an intraperitoneal organ. The bladder wall grows thinner in proportion to the quantity of urine, and the flexibility of its muscular fibers decreases. The superior and posterior walls (bladder dome) are anatomical areas with the least resistance. Vesical pathologies determining a decline in wall strength (inflammatory, tumor, scarring processes) favor surprisingly severe lesions following minor traumas. Neurological lesions of the vesical wall lower its ability to distend and reduce muscle tone, consequently allowing the accumulation of a large amount of urine. It is the case of neurogenic bladder patients. In pregnancy, the raised estrogens cause marked hyperemia, vasodilatation, and increased tortuosity of the blood vessels of the genitourinary system. Moreover, as it grows, the gravid uterus mechanically lifts the bladder into the abdomen and more anteriorly, thus making it more susceptible to spontaneous or inflicted injury.

### 28.3.3 Clinical Presentation

Clinical diagnosis is challenging when bladder rupture occurs during delivery and early puerperium. The pain in the second and third stages of labor is so severe that the pain from rupture can-

not be felt separately. So, the patient may present late with features of renal failure and urinary ascites. Palpation of the involuting uterus is an important part of the aftercare of the puerperal patient. Delay in the descent of the fundus is often an indication that the bladder is not being emptied. After uneventful labor, ascites, and azotemia in the early postpartum raise suspicion of intraperitoneal rupture of the bladder. Tachycardia is followed by hypotension [113, 124, 134]. Difficulties in passing urine in the postpartum period occur, but the oliguria or anuria with abdominal pain should raise a suspicion of bladder injury. Abdominal pain is initially in the lower abdomen, and macrohematuria can be present with low back pain. Puerperal presentation is mostly within 24 h, although some cases were diagnosed several days after delivery [106].

Abdominal examination reveals a distended abdomen with dullness on percussion. Signs of peritoneal irritation or peritonitis could be absent initially but develop during the first 1–4 days after bladder injury [135]. Low abdominal pain can temporarily improve with a Foley urethral catheter placement and worsen over subsequent days, especially when the catheter is removed [106, 136]. Blood on the external meatus or gross hematuria is common with bladder rupture or larger perforation. With oliguria, macrohematuria is confirmed with a Foley urethral catheter [120]. Bladder trauma should be excluded with unexplained hematuria during pregnancy, even without a history of trauma. Unfortunately, nulliparous women may confuse hematuria with lochia. Fever is not present initially [113]. Vaginal examination reveals a healthy episiotomy wound (if made), lochia rubra, and closed internal cervical ostium [113, 124]. Uterine size should correspond to weeks of pregnancy or involution during the early postpartum period with no rigidity or pain on palpation. The normal fetal position minimizes the possibility of uterine rupture.

If fetal distress accompanies clinical presentation, uterovesical ruptures are likely [120].

An unrecognized bladder injury during CS can lead to a vesicovaginal fistula or vesical calculi without urinary incontinence from a vesicouterine fistula [137, 138] or menuria without



urinary incontinence secondary to a vesicouterine fistula. Gross hematuria can present even several years after CS [139]. The nonoperative causes, such as inflammatory bowel diseases, can present as recurrent UTIs during pregnancy, such as hemorrhagic cystitis, despite antibiotic prophylaxis [140].

28.3.4 Differential Diagnosis

Due to commonly nonspecific symptomatology, the diagnosis has rarely been suspected initially [141]. When patients develop acute renal failure, prerenal and obstructive causes must be excluded. An important cause of prerenal azotemia in pregnancy is uterine hemorrhage, as in placental abruption. Infectious causes of acute renal failure in pregnant women include acute pyelonephritis and septic abortion. The clinical presentation of both conditions should be apparent, and appropriate diagnosis and treatment should be promptly instituted. Renal cortical necrosis is another frequent cause of renal failure during pregnancy. It must be differentiated from the many causes of acute tubular necrosis associated with pregnancy. Postpartum renal failure in previously healthy subjects is mostly associated with preeclampsia or hypertension, HELLP syndrome, hemolytic uremic syndrome, or thrombotic thrombocytopenic purpura [142]. Doppler US should exclude renal hypoperfusion due to a renal vascular occlusion. The normal platelet count and hemoglobin levels exclude pregnancy-associated microangiopathy, such as hemolytic uremic syndrome.

Another common working diagnosis in patients with acute postpartum pain is spontaneous uterine rupture (see Chap. 16) [124] because induced vaginal delivery increases the rate of intraperitoneal bladder rupture commonly associated with uterine rupture [121, 143]. A wrong working diagnosis of uterine rupture is supported by the fact that most develop acute suprapubic pain, oliguria/anuria, and free intraperitoneal fluid. The differential diagnoses are summarized in Table 28.4.

**Table 28.4** Differential diagnosis of spontaneous bladder rupture

|                             |
|-----------------------------|
| Acute renal failure         |
| Spontaneous uterine rupture |
| Urinary tract infection     |
| Placental abruption         |
| Acute pancreatitis          |
| Postpartum hemorrhage       |
| Small bowel injury          |
| Large bowel injury          |

28.3.5 Diagnosis

28.3.5.1 Laboratory Findings

Profound disturbances in serum electrolytes and acid-base status (elevated serum urea, creatinine, and potassium, decreased serum sodium and CO<sub>2</sub> content, and development of metabolic acidosis) are consistent with intraperitoneal bladder rupture. When urine enters the peritoneal cavity, reverse autodialysis occurs. Urea and creatinine diffuse down their concentration gradients into the blood. The rapid early rise in creatinine suggests peritoneal urinary resorption (pseudo-renal failure) rather than true acute renal failure. The serum urea and creatinine are elevated in 45% of patients who present within 24 h of bladder rupture and in nearly 100% of the patients who present 24 h after bladder rupture, with higher urea levels due to high peritoneal absorption [144].

The hyponatremia with elevated serum creatinine levels, consistent with dehydration and renal failure, suggests urinary peritonitis [111], especially after uneventful vaginal delivery [134].

Biochemical analysis of ascitic fluid confirms urine by testing ascitic fluid creatinine, similar to urine creatinine [113]. The urinary sediment demonstrates hematuria and leukocytes [106].

Features common to intraperitoneal bladder rupture are: (1) urinary ascites, (2) paralytic ileus, (3) acute renal failure secondary to systemic reabsorption of urea and creatinine, (4) hyperkalemia due to acute renal failure, and (5) metabolic acidosis [126].

### 28.3.5.2 Imaging

US and saline sonocystography are not very sensitive in diagnosing bladder rupture. US is helpful with previous normal US findings. Free fluid in the abdomen should raise suspicion of intraperitoneal rupture. Clinical or radiologic findings suggesting bladder rupture (e.g., pelvic ring disruption, obliteration of pelvic fat planes) mandate a retrograde cystogram with a maximally distended bladder and a postevacuation film. Through a Foley urethral catheter, at least 250–300 ml of contrast material into the urinary bladder is instilled (as much as the alert patient will tolerate), and intraperitoneal contrast leakage is detected (Fig. 28.21).



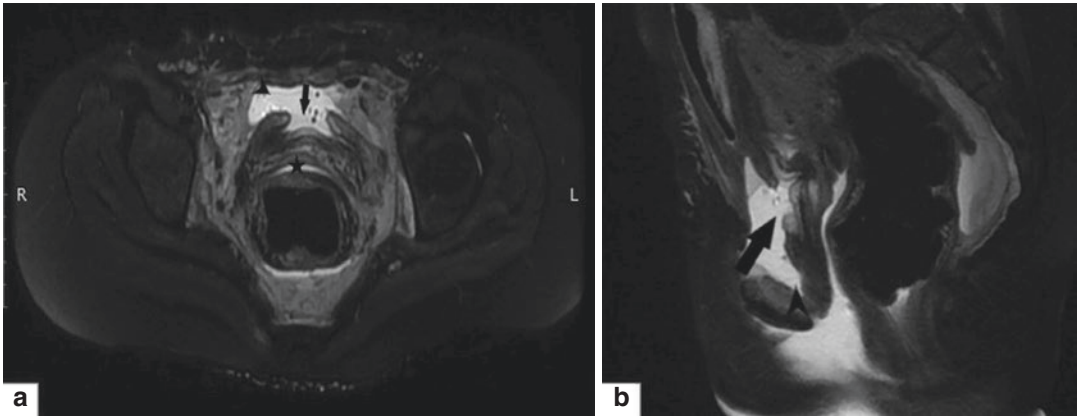
**Fig. 28.21** Retrograde cystogram of 16 weeks pregnancy shows contrast extravasation from the bladder into the peritoneal cavity. (Reproduced with permission from [133])

Though retrograde cystography is considered the investigation of choice for establishing the type of bladder rupture in stable nonpregnant cases, contrast studies are avoided during pregnancy.

In the general population, CT cystography has the same sensitivity as plain X-ray cystography (90%). It is recommended to rule out other visceral injuries [145]. Impaired renal function is not a contraindication for CT cystography. It is done by retrograde administration of 300–350 ml diluted (10%) contrast with saline into the urinary bladder through a urethral catheter, followed by CT of the lower abdomen and pelvis. It detects the rupture site and even small rent due to bladder distension (Fig. 28.22). However, in the excretory phase, a delayed contrast CT does not show contrast extralumination through the small bladder rent, covered by a blood clot or omentum [126, 146]. Furthermore, oral contrast for bowel opacification may obscure and confuse the findings when a subsequent plain film cystogram is needed. The one exception is the potentially unstable patient, where the contrast should be diluted to 5% and instilled into the bladder before any CT cuts are obtained. Air can substitute a bladder contrast agent.



**Fig. 28.22** CT cystogram after uneventful vaginal delivery shows extravasation of contrast from bladder forming fistulas from the bladder dome to intraperitoneal space [134]



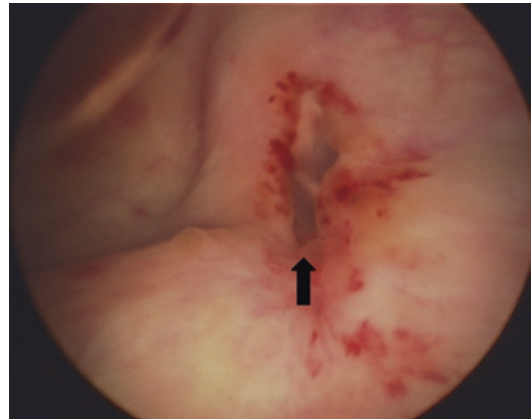
**Fig. 28.23** MRI of the pelvis. T2-weighted fat saturated in (a) axial and (b) sagittal planes show a defect in the anterior urinary bladder wall (*black arrow*) with extraperi-

toneal fluid collection (*arrowhead*). Note the normal upper part of the vagina (\*). (Reproduced with permission from [147])

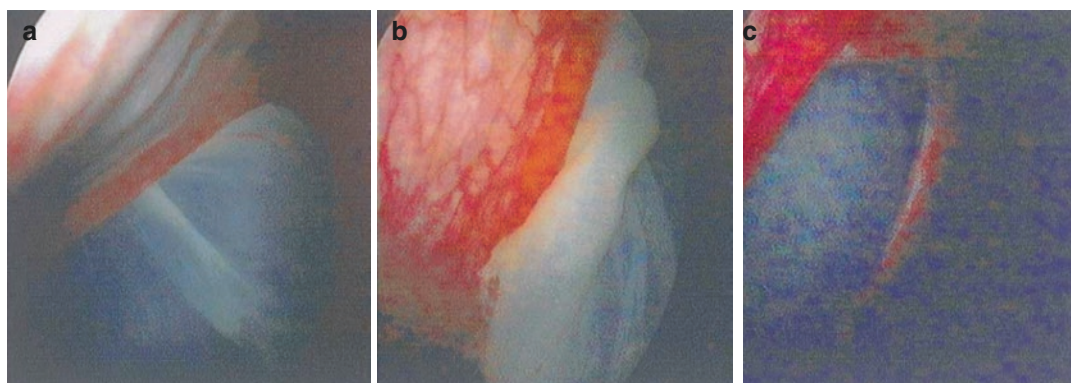
Emergent MRI detects the extralumination and exact location of the rupture (Fig. 28.23).

### 28.3.5.3 Cystoscopy

Cystoscopy can define the location and size of urinary bladder injury instead of retrograde cystography (Fig. 28.24). Cystoscopy is indicated with gross hematuria [106, 121]. If the enterovesical fistula is suspected, cystoscopy can reveal the presence and location of the vesical fistulous opening [140]. Enterovesical fistula can be confirmed by charcoaluria following oral charcoal administration [140]. Even amniotic sac protrusion can be seen through the vesicouterine fistula (Fig. 28.25). Follow-up cystoscopy (after 2 weeks) shows intact bladder mucosa [106].

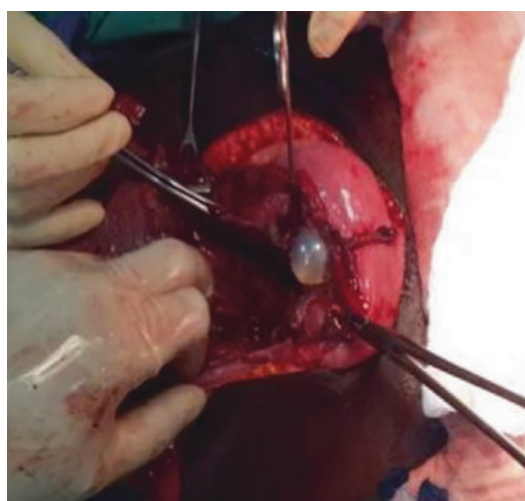


**Fig. 28.24** Cystoscopic view of bladder injury 1 × 1 cm at the left bladder dome, 4 days after cesarean section. (Reproduced with permission from [106])



**Fig. 28.25** (a) Cystoscopic view: herniation of amniotic sac in the bladder. Evidence of a whitish, roundish neoforation with a perfectly smooth surface protruding in the bladder; (b) gradual reduction of the herniation of the

amniotic sac during bladder filling; (c) the complete disappearance of the herniation showed the oval vesical tear of the hernial neck. (Reproduced with permission from [139])



**Fig. 28.26** The balloon of the Foley's urethral catheter visible through the posterior bladder wall defect after the delivery. (Reproduced with permission from [148] under the CC Attribution License)

## 28.3.6 Treatment

Bladder injury can be confirmed or recognized intraoperatively with findings of bladder perforation: the extravasation of urine, a visible laceration, the appearance of a Foley urethral catheter (Fig. 28.26), a sudden increase in bleeding from the wound, and bloody urine in the urinary bag. Intraoperative intravesical instillation of methylene blue or indigo carmine through the Foley urethral catheter reveals the perforation location.

There are no guidelines for specific antibiotic therapy and duration of antibiotic therapy in the pregnant population with urinary bladder rupture. Therefore, antibiotics should follow recommendations for the general population for antibiotics within the FDA classes B and C.

### 28.3.6.1 Spontaneous Bladder Rupture

#### Extraperitoneal Bladder Rupture

Extraperitoneal ruptures are mostly managed conservatively with Foley urethral catheter drainage of the bladder for 10–14 days. No firm guidelines exist about antibiotic therapy for spontaneous urinary bladder rupture. For traumatic injury 7-day course of antibiotics is recommended. Many empirical antibiotic classes for the lower urinary tract are FDA category C. Therefore, cephalosporins, nitrofurantoin, or penicillins should be used.

#### Intraperitoneal Bladder Rupture

Intraperitoneal ruptures of the urinary bladder require urgent surgical repair. At emergency laparotomy, the rupture site is identified, sometimes immediately, sometimes with methylene blue over Foley urethral catheter.

See “Uterovesical Rupture” for operative details. Early management reduces infectious complications and adverse outcomes [126].



### Uterovesical Rupture

A Pfannenstiel incision or lower midline laparotomy depends on the accuracy of the preoperative diagnosis. The further procedure depends on whether the fetus has been delivered. The fetus should be delivered first if it is still in the pelvis. It can be outside the uterus, or only part of the fetus can lie outside it. Even the fetus can go first through the rent of the uterus and then through the rent in the urinary bladder. In this situation, the bladder is opened completely, and the fetus is delivered from inside the bladder (Fig. 28.27a). In such situations, the posterior wall of the bladder and the anterior wall of the uterus rupture (Fig. 28.27b).

Both ureteral orifices should be catheterized with a 5Fr feeding tube to confirm clean urine. The integrity of the ureters is documented with IV instillation of indigo carmine dye demonstrating normal urine production from the ureteral orifices [120]. Injuries involving ureteric orifices and the trigonal area may require ureteric stenting, ureteroneocystostomy, etc. Afterwards, the laceration of the bladder wall is closed in two layers with 2-0 or 3-0 running absorbable sutures. The first bite can incorporate all layers, including the bladder mucosa, although many omit the bladder mucosa and include only the submucosa and muscular layers. The second imbricating layer may be a parallel Lembert or a perpendicular Connell stitch. Foley urethral catheter is kept for 10–14 days to keep the bladder compressed. If the suprapubic drain (cys-

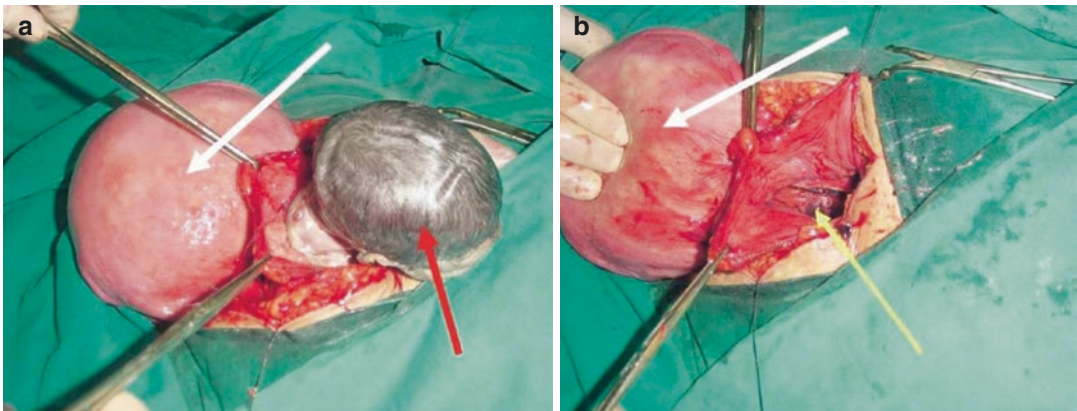
tostomy) is inserted, it is clamped on the tenth day and removed on the 12th day. Urethral Foley's catheter is removed on the 14th day. Antibiotics against *E.coli* are used, the most common pathogen in the female population. IV antibiotics are used for febrile patients who cannot tolerate peroral feeding followed by peroral antibiotics.

The uterus is then reapproximated using a two-layer closure technique [121]. Sometimes, the repair is complex because uterine rents are commonly multiple with bladder injury [108]. An omental flap can be mobilized and positioned between the opposing suture lines before closing the abdominal cavity [108, 120] to reduce the possibility of fistulas. Primary bladder repair is successful, with a return of normal bladder function [120].

### 28.3.6.2 Traumatic Bladder Rupture/ Injury

#### Cesarean Section

An isolated small tear at the bladder dome is sutured primarily without additional evaluation. A larger tear may be associated with a concomitant injury to the ureter, particularly if the damage involves the posterior bladder wall, approximates the ureteral orifice, or is associated with the lateral extension of the uterine incision. Ureteral catheterization is advisable to identify the orifices, even at the cost of expanding the primary bladder tear toward the trigone.



**Fig. 28.27** (a) Dead fetus in the bladder. Uterus (white arrow); head of the fetus (red arrow). (b) Rupture of posterior bladder wall and uterus. Uterus (white arrow); rupture site (yellow arrow). (Reproduced with permission from [121])



See “Uterovesical Rupture” for operative details. After a repair, a suprapubic drain is recommended for large ruptures, but a large Foley urethral catheter would be sufficient for smaller injuries.

### Blunt Abdominal Trauma

Bladder contusions and most extraperitoneal ruptures are mostly managed conservatively with continuous bladder drainage for 7–10 days [149]. Most intraperitoneal and extensive extraperitoneal ruptures need surgical repair [149]. See “Uterovesical Rupture” for operative details. Suppression of the inflammation lowers the production of prostaglandins, which lowers the possibility of spontaneous abortion or preterm labor (see Chap. 4).

## 28.3.7 Prognosis

### 28.3.7.1 Maternal Outcome

Preoperative diagnosis avoids reintervention and readmission, decreasing cost and morbidity. Neither severe postoperative complications nor sequelae are noticed after managing the bladder ruptures or injuries [148]. Even a normal postrepair cystogram could result in transient (up to 6 months) loss of bladder sensation [150]. Urodynamic studies are then indicated, and treatment is based on their findings.

### 28.3.7.2 Fetal Outcome

An objective fetal outcome is unknown due to exceedingly rare cases before labor or puerperium. Prolonged urinoma/urinary peritonitis does not lead to spontaneous abortion or preterm labor [115, 117, 151], unlike peritonitis of gastrointestinal origin.

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## Abstract

Renal trauma during pregnancy results from blunt, penetrating, or iatrogenic trauma. Blunt trauma results from falls, domestic violence, or motor vehicle accidents (MVA). Traumatic renal rupture is most common after MVA. CT urography is diagnostic. In stable patients, abdominal MR has similar accuracy. Nonoperative management mostly suffices. During operation, kidney conservation methods are successful. Completely destroyed kidney with hilar bleeding mandates nephrectomy. Renal artery aneurysms (RAA) are slightly more common on the left side, contrary to the general population. Increased rate of RAA rupture results from an increased intravascular volume with increased systemic blood pressure, increased blood flow through kidneys (30–50% in the first trimester) with increased pressure in renal arteries, increased intraabdominal pressure, gravid uterine compression on the infrarenal aorta and right renal artery,

and weakened structure of the major arteries following increased steroid production. Transabdominal ultrasound with Doppler mode is diagnostic. Angiography is diagnostic and therapeutic with the placement of a stent. RAA before or during pregnancy should be treated with endovascular techniques. Ruptured RAA is treated surgically with aneurysm resection and reconstruction or nephrectomy.

## 29.1 Traumatic Renal Injury/Rupture

### 29.1.1 Incidence and Risk Factors

Renal trauma during pregnancy results from (1) blunt, (2) penetrating, or (3) iatrogenic trauma. Blunt trauma results from falls, domestic violence, or motor vehicle accidents (MVA). Traumatic renal rupture is most common after MVA [1, 2]. WF Gemmill and TA Martin (York

Hospital, York, Pennsylvania, USA) described one of the first cases in 1933 [1] after MVA. The ectatic collecting system associated with pregnancy increases the tearing rate, especially with trauma resulting in increased intra-abdominal pressure [2].

### 29.1.2 Clinical Presentation

See Sect. 29.2.3. The main symptom is macrohematuria [2], sometimes revealed after the urinary catheter placement [3].

### 29.1.3 Differential Diagnosis

The diagnosis of renal injury after traumatic lumbar pain, primarily if associated with macrohematuria, is straightforward. Traumatic renal injury or rupture is rarely isolated during maternal blunt abdominal trauma. Therefore, other intra-abdominal injuries should be sought (see Chap. 25).

### 29.1.4 Diagnosis

#### 29.1.4.1 Laboratory Findings

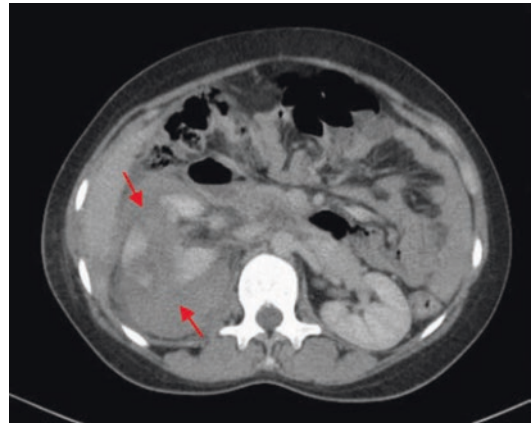
In isolated renal trauma, depending on the severity of bleeding, a drop in serum Hgb values could be present [1, 3]. Urinalysis can reveal microhematuria, resolving on repeated tests during the next several days [1].

#### 29.1.4.2 Transabdominal Ultrasound

Transabdominal ultrasound (US) is rarely diagnostic because it is challenging to differentiate urine from blood. Also, it is difficult to assess the severity of injuries, findings that are important for the management plan.

#### 29.1.4.3 Abdominal CT

The preferred imaging study for renal trauma is contrast-enhanced computed tomography (CT) [1, 3]. It provides the most definitive staging: parenchymal lacerations and perirenal are clearly defined (Fig. 29.1). Extravasation of contrast-enhanced urine, associated injuries to bowel, pan-



**Fig. 29.1** A 6 cm-sized laceration in the right kidney lower pole (AAST Grade IV injury) with perinephric hematoma (arrows). (Reproduced with permission from [3])

creas, liver, spleen, and other organs, and the degree of retroperitoneal bleeding can be assessed.

#### 29.1.4.4 Abdominal MRI

Magnetic Resonance Imaging (MRI) is useful in stable patients. Benefits include clarification of equivocal cases, identifying urine leaks, either in a delayed presentation, and monitoring other complications of renal trauma. MRI has high accuracy in defining injuries specific and nonspecific for pregnancy. Placental injuries and hematomas, in particular, are better seen on MR than on CT, owing to its superior contrast resolution [4].

### 29.1.5 Treatment

Management strategies depend on the severity of (1) bleeding, (2) urinary extravasation, and (3) associated intra-abdominal injuries. Renal trauma management has shifted from immediate surgical exploration to nonoperative management with kidney preservation unless fetal distress develops. In 1933, kidney injury was repaired with sutures, and its function was salvaged [1].

### 29.1.6 Prognosis

Isolated renal injuries do not result in maternal mortality. After maternal blunt abdominal

trauma, preterm labor results from various causes (see Chap. 4) [1].

## 29.2 Renal Artery Aneurysm Rupture

### 29.2.1 Historical Perspective and Incidence

In the general population, renal artery aneurysms (RAA) show a slightly different natural history than other visceral artery aneurysms, with a significantly lower risk of rupture and a considerably lower mortality rate. The most frequent is splenic artery aneurysm rupture (see Chap. 24). Ludovici Rouppe described the first report of ruptured RAA in 1770. It was the case of a sailor who fell onto his right flank. After 9 days, he felt significant pain. He died due to (pseudo)aneurysm rupture [5]. A. E. Chisholm (Dundee Royal Infirmary Maternity Department, Dundee, Scotland) described the first case in 7 months of pregnancy in 1926 [6]. The patient was operated on in profound hemorrhagic shock and died. The fetus was also dead. Previously, when the information on the disease came from autopsy, it was considered extremely rare in the general population, with an incidence of 0.01–0.09% [7]. With the introduction of visceral angiography, the diagnosis of RAA became more frequent (0.3–2.5%, or even higher) [7]. However, these figures

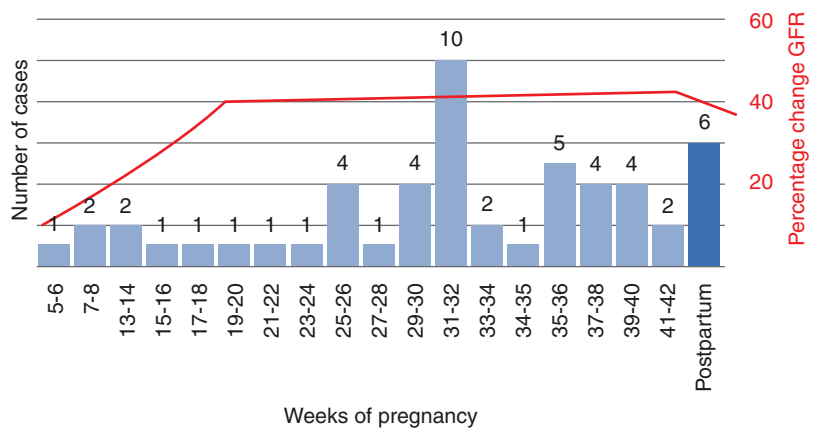
do not reflect the true incidence of RAA in the general population because an RAA may have caused the symptoms that brought these patients to renal angiography. Until 2017, 53 cases have been reported during pregnancy [8].

RAAs are commonly on the right side in the general population ( $\approx 60\%$ ), probably due to the higher incidence of fibrodysplasia on that side (68%). Women account for 72% [7]. Before 1970, reported rupture of RAA in pregnancy was mainly on the left side and during the third trimester, while after 1970, there was slightly less left-sided predominance [9]. The higher incidence during pregnancy may be due to increased reporting of such incidents.

It appears to be an RAA shift from a right-sided predilection in nonpregnant women to a slight left-sided (1.4: 1) in pregnancy [8].

Left-sided predominance more than 50 years ago could be due to the change in etiologic factors during the last decades (nutrition, screening, etc.). Incidence during trimesters is 5.7%, 20.7%, and 62.3%, with high incidence in the early puerperium [8]. The incidence correlates with changes in the glomerular filtration rate (Fig. 29.2).

**Fig. 29.2** Correlation of incidence of RAA rupture and GFR during pregnancy. RAA renal artery aneurysm, GFR glomerular filtration rate. (Modified and reproduced with permission from [8])



**Table 29.1** Risk factors for RAA rupture in pregnancy [8, 11]

| Local                    | Systemic                         |
|--------------------------|----------------------------------|
| Incomplete calcification | Arterial hypertension            |
| Size >2 cm               | Multiparity                      |
| Progressive enlargement  | Third trimester/early puerperium |
| Renal embolization       | Ehlers-Danlos syndrome           |

### 29.2.2 Etiopathogenesis

Over 50% of ruptured arterial aneurysms in women under 40 are pregnancy-related [10]. Although pregnancy is probably not associated with an increased RAA incidence, it is associated with a higher rupture rate (Table 29.1).

Until 1997, the proportion of patients during pregnancy and puerperium in all surgically treated ruptured RAA was 59% [11]. Some lesions may result from congenital defects in the elastic tissue of the media, arteriosclerosis, especially in older patients, postinfectious or post-traumatic lesions, or fibromuscular dysplasia [12]. Fibromuscular dysplasia can cause stenosis and aneurysmal dilatation of the renal artery. It occurs most frequently in young women. Patterson reported the presence of “muscular intimal thickening” proximal to the aneurysmal region in a renal artery that ruptured during pregnancy [13]. RAA associated with fibromuscular dysplasia is found bilaterally in 7–30%, unilaterally (multiple) in 7–13%, and extrarenally in 2.5–10% [14]. Positive family history is also a risk factor [15]. Hemodynamic changes such as increased intravascular volume, cardiac output, intra-abdominal pressure in pregnancy, and hormonal changes predispose to rupture [16] as in splenic artery aneurysms (see Chap. 24). The increased risk in the third trimester of pregnancy is due to (1) expanded intravascular volume with increased systemic blood pressure; (2) rapid increase of blood flow through kidneys (30–50% in the first trimester)

with increased pressure in renal arteries; (3) increased intra-abdominal pressure, especially during labor; (4) gravid uterine compression on the infrarenal aorta and right renal artery due to the physiological clockwise rotation; and (5) weakened structure of the major arteries following increased steroid production [17–19]. The mechanical–physiological changes remain during early puerperium (Fig. 29.2), and all postpartum patients presented within 7 days and 50% within 24 h of labor.

The mechanism of RAA rupture in the first trimester of pregnancy remains unclear. The renal plasma flow and glomerular filtration rate in pregnant women in the first trimester rapidly increase to about 30–50% above the nonpregnant level; thus, increased blood flow to the kidneys may increase the pressure in the arteries, resulting in RAA expansion and rupture [20]. Parity is a risk factor for RAA rupture (71.4% were multiparous [8]). Multiparity might cause irreversible vessel wall damage, promoting rapid aneurysm growth and rupture [21]. Furthermore, multiparas are older, and the advancing age carries a biological impact on atherosclerosis and vessel degeneration. Moreover, RAAs can thrombose or release emboli, obstructing smaller renal arteries and causing multiple renal infarctions.

As in the general population, RAAs in pregnancy are predominantly saccular [8].

### 29.2.3 Clinical Presentation

Clinical presentation differs between ruptured and unruptured RAA. Typically, the patient with an RAA is asymptomatic. If symptomatic, the patient complains of vague flank or upper abdominal pain that can progress to more severe pain due to enlargement of the RAA. The characteristic presentation of ruptured RAA is sudden (60.4%), severe (62.3%), unilateral flank pain commonly followed by hemorrhagic shock with

fainting attacks [8]. It is called *Wunderlich syndrome*, in which spontaneous nontraumatic renal hemorrhage occurs in the subcapsular and perirenal spaces. Collapse is present with large retroperitoneal hematomas. Without peritoneal rupture, the retroperitoneum has a tamponade effect. There is no associated history of trauma or fever [22], and macrohematuria can be present but is not common [8]. Gross hematuria and clot retention are signs of intraparenchymal RAA rupture into the collecting system, renal embolization, or infarction [23]. Therefore, Wunderlich syndrome is clinically characterized by *Lenk's triad*:

- Acute flank pain,
- Flank mass,
- Hypovolemic shock.

In the absence of rupture, physical findings may merely reveal arterial hypertension (15–75%) [24, 25] or abnormal pulsations or bruits. There are no symptoms and signs of labor or vaginal bleeding, and the cervix is closed and uneffaced [8, 22]. Severe bleeding results in pallor, cold sweat, and hypotension with tachycardia [8]. An abdominal examination reveals generalized or localized tenderness. A tender mass can be palpated on the affected side [13], and if the retroperitoneal mass/hematoma is large, it may displace the gravid uterus to the opposite side [16, 26]. The uterus corresponds to the duration of pregnancy. Fetal cardiac activity can be absent depending on the duration and severity of bleeding/retroperitoneal hematoma [22].

## 29.2.4 Differential Diagnosis

Other urologic diagnoses should be excluded with isolated flank pain, primarily upper urinary tract infection, urolithiasis, or renal angiomyoli-

poma. The spontaneous liver rupture (see Sect. 26.1) could be found on the right side, while spontaneous splenic rupture (see Chap. 24) dominates on the left. The differential diagnosis depends on whether flank pain is associated with bleeding (Table 28.2). A differential diagnosis of placental abruption or uterine rupture is considered with fetal distress or signs of hemodynamic instability. A normal vaginal examination excludes many gynecologic/obstetric causes because the more common causes of hemorrhagic shock during pregnancy are obstetric (placental abruption, placenta previa, ruptured uterus, and ectopic pregnancy in early gestation).

## 29.2.5 Diagnosis

The contralateral kidney and eventual RAA status should be checked because some degree of congenital/acquired systemic or kidney impairment is common. It is common with Ehlers–Danlos syndrome, tuberous sclerosis, periarteritis nodosa, etc. The status of the contralateral kidney and potential contralateral RAA (in the general population, 10–20% [7]) define treatment strategies.

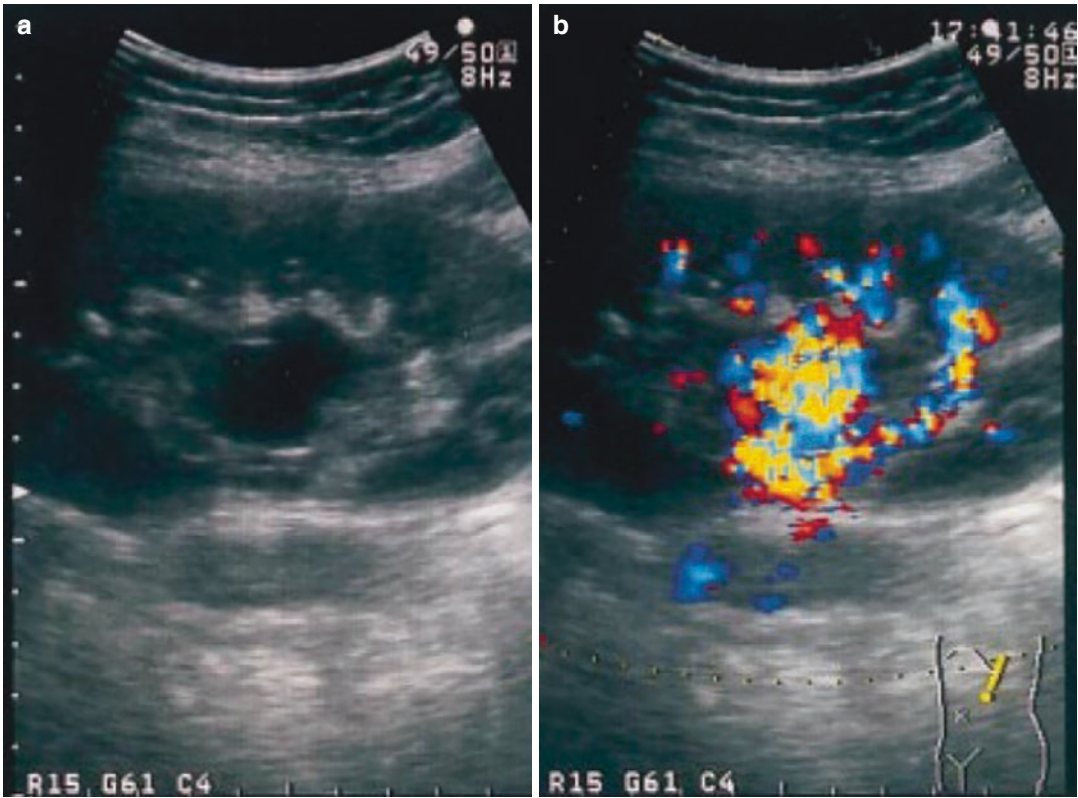
### 29.2.5.1 Laboratory Findings

The unruptured RAA has microscopic hematuria in 33–45% of cases [25, 27, 28], whereas ruptured RAA reveals anemia, macrohematuria, or microhematuria [8, 16]. Due to sudden onset and abrupt hypotension, laboratory tests are seldom performed [15, 22].

### 29.2.5.2 Transabdominal Ultrasound

The transabdominal ultrasound (US) is the first imaging method for stable and unstable patients. Without Doppler mode, intrarenal uncalcified RAA can be mistaken for hydronephrosis (Fig. 29.3a). A Doppler US can define





**Fig. 29.3** (a) Sonogram of the left kidney shows “hydronephrosis.” (b) A color Doppler in the same plane shows an intrarenal aneurysm. (Reproduced with permission from [29])

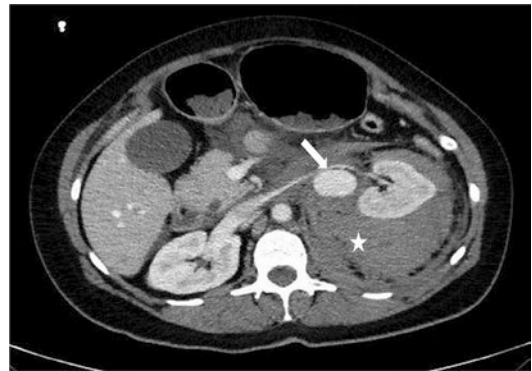
the location and dimension of the RAA (Fig. 29.3b) and confirms arterial patency or active bleeding [15, 29].

#### 29.2.5.3 Abdominal CT

Native or contrast-enhanced abdominal CT is performed (sensitivity 94%) when US (sensitivity 70%) is nondiagnostic. Contrast-enhanced abdominal CT is common after preterm delivery or CS when a diagnosis is unknown. CT angiography defines the location of the bleeding, RAA characteristics, and the extension of the hematoma (Fig. 29.4). The downside is that it cannot be used for selective embolization or stenting of the ruptured RAA.

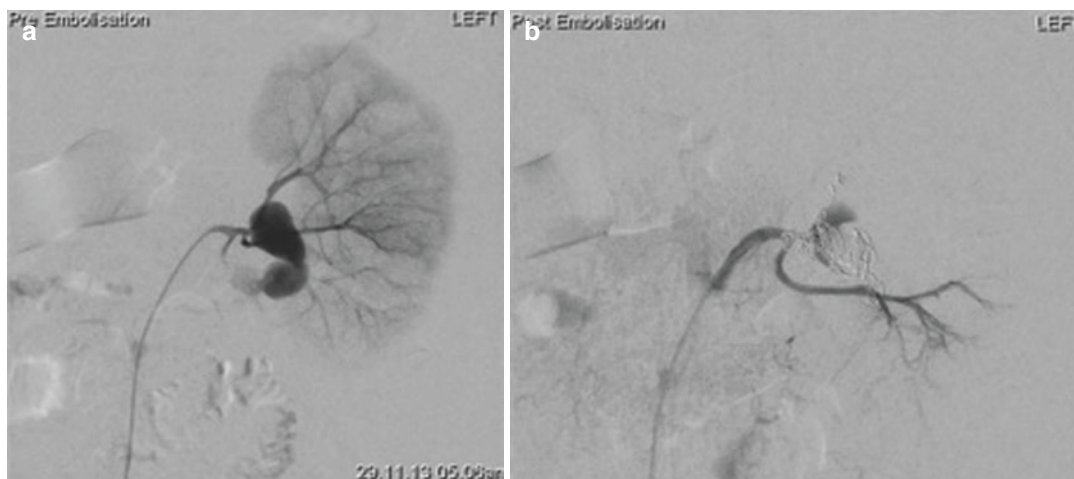
#### 29.2.5.4 Angiography

Digital subtraction angiography precisely defines the location of an RAA, the location of rupture



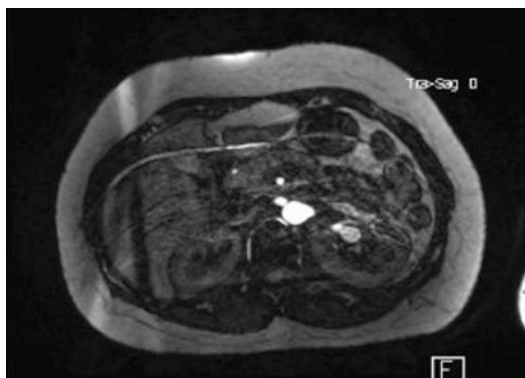
**Fig. 29.4** Contrast-enhanced abdominal CT shows a left renal artery aneurysm (*white arrow*) and a large retroperitoneal hematoma (*white star*). (Reproduced with permission from [30])

with leakage (Fig. 29.5). If indicated, in the same act, the stent-graft can be placed over an aneurysm covering the rupture site (see Sect. 29.2.6.2).



**Fig. 29.5** (a) Preembolization angiography shows bleeding left renal artery. (b) Postembolization angiography of the left renal artery shows aneurysm securement resulting

in kidney infarction. (Reproduced with permission from [31] under the CC BY-NC-ND 4.0)



**Fig. 29.6** MRI angiogram at 9 weeks of pregnancy shows a 1.4 cm aneurysm at the bifurcation of the left renal artery involving the origin of the lower pole branch. (Reproduced with permission from [32])

### 29.2.5.5 Abdominal MR

Abdominal MR is rarely performed because it is frequently unavailable in emergency settings [31] and unsuitable for hemodynamically unstable patients. Without contrast, abdominal MR (Fig. 29.6) is used for symptomatic, unruptured RAAs [15].

## 29.2.6 Treatment

The treatment of the nonpregnant and pregnant populations is slightly different. Treatment of incidental contralateral RAA in the general population is not mandatory; active surveillance is safe in most cases [7]. Nevertheless, abrupt onset of RAA progression and rupture, increased risk during pregnancy, lead to high morbidity and mortality and warrant early repair of an RAA in women planning a pregnancy.

### 29.2.6.1 Conservative Treatment

With asymptomatic RAA during pregnancy, conservative treatment is not recommended. In patients who do not consent to the operation, surveillance is indicated if [16]:

- RAA noncalcified,
- RAA <2 cm in diameter,
- RAA not increasing in size,
- The presence of contralateral kidney.

Arterial hypertension should be corrected to lessen the possibility of RAA rupture. Frequent US surveillance is mandatory. Pregnant patients and their families should be instructed to immediately go to the hospital if lumbar pain or hematuria occurs.

### 29.2.6.2 Endovascular Treatment

If the anatomy is favorable, endovascular procedures should be performed on the hemodynamically stable patient. Two endovascular procedures are used: embolization [19, 31, 33] and stent-graft placement. The location of an RAA is important because embolization of an aneurysm of the main renal artery or at the bifurcation carries a high risk of complete occlusion of the renal artery and atrophy of the kidney [17]. Elective endovascular management does not reduce in-hospital mortality with ruptured RAA in the general population, although it leads to a lower complication rate and shorter length of stay [34]. Hypothetically, endovascular techniques could be bridge therapy until delivery.

Ideally, stents and coils covering the RAA should be used. If technically challenging, embolization of the main renal artery in hemodynamic instability could stabilize the patient enabling subsequent nephrectomy [12]. The lower success rate, stent migration, or leakage is present in the pregnant population [30] as in the general population. Unsuccessful stent placement necessitates nephrectomy [30] or open aneurysm repair (see Sect. 29.2.6.4).

### 29.2.6.3 Surgical Treatment

#### Operative Principles

Hemodynamic instability with confirmed or suspected RAA mandates exploratory median laparotomy with surgical treatment of ruptured

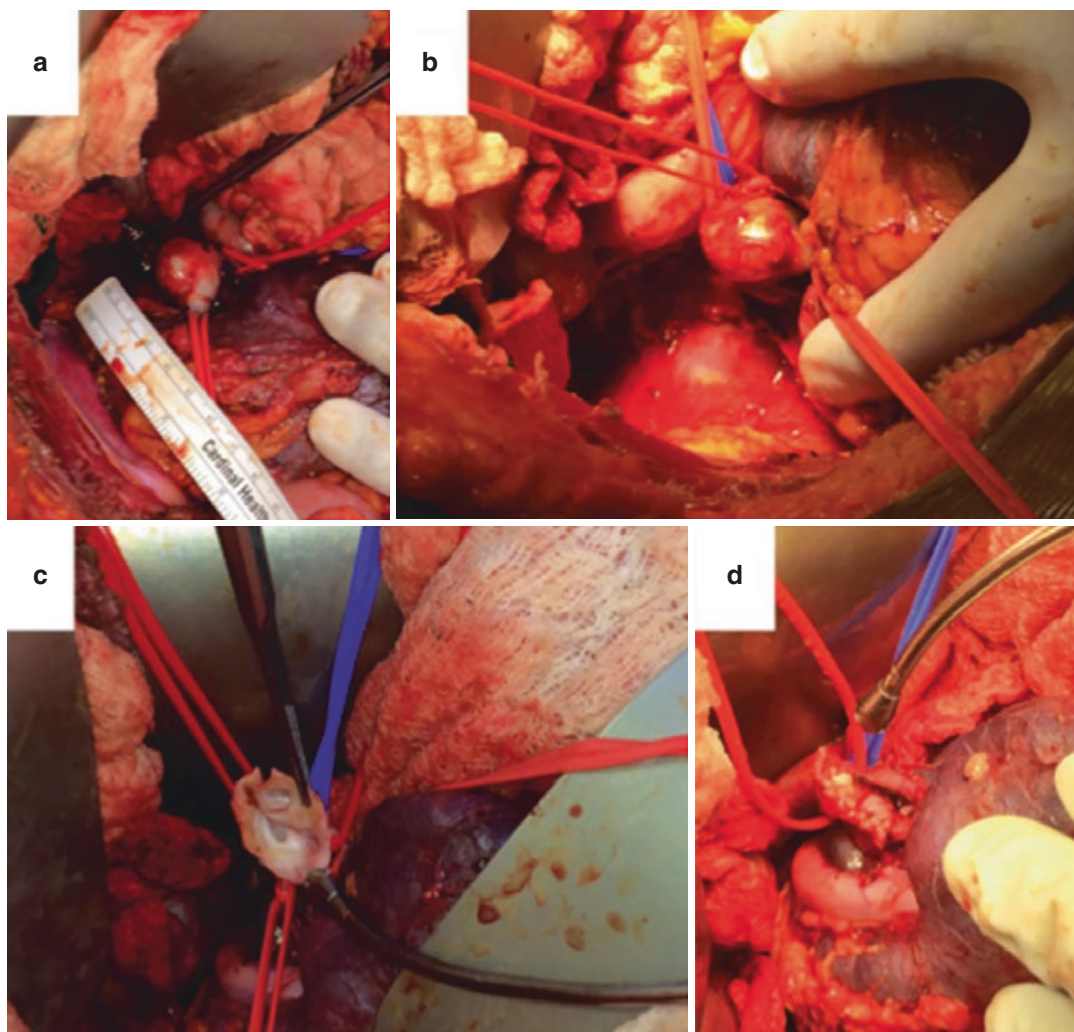
RAA. Simultaneous CS is performed if indicated by the obstetrician. For stable patients with unfavorable localization of the ruptured RAA, and no fetal distress, a lumbotomy is recommended.

Extension of a large retroperitoneal hematoma on the affected side depends on the duration and the severity of the bleeding. It can expand below the diaphragm to the pelvis and even cross the midline [22]. Large hematomas may displace the gravid uterus to the opposite side [35, 36]. The hematoma is nonexpanding and nonpulsatile [22]. In the setting of ruptured RAA, information on preoperative (bilateral) renal function is usually incomplete.

Reconstructive options include (1) aneurysmal resection with end-to-end anastomosis (Fig. 29.7) and (2) extracorporeal vascular reconstruction with autotransplantation. The salvage of the kidney in the emergency bears no additional surgical risk and can be performed without significantly extending the duration of surgery. If the RAA is large and the kidney is destroyed, (partial) nephrectomy is the only option.

In 1960, the mortality after nephrectomy in all groups with RAA was 5.3–6%. In comparison, organ-preserving methods had 53–60% [37]. It was not until 1981 that Love et al. reported the first organ-preserving surgery and Proabulos et al. in 1997, the first endovascular treatment [33]. Nephrectomy was predominant until 1997 [8]. Until 2001, salvage of the kidney was 26%, either by in situ repair of the renal artery or by ex situ repair and kidney autotransplantation [38]. Since then, endovascular treatment has been successfully performed [19, 31, 33]. Since the year 2000, an equal share of nephrectomy, renal artery reconstruction, and endovascular techniques has been employed [8].

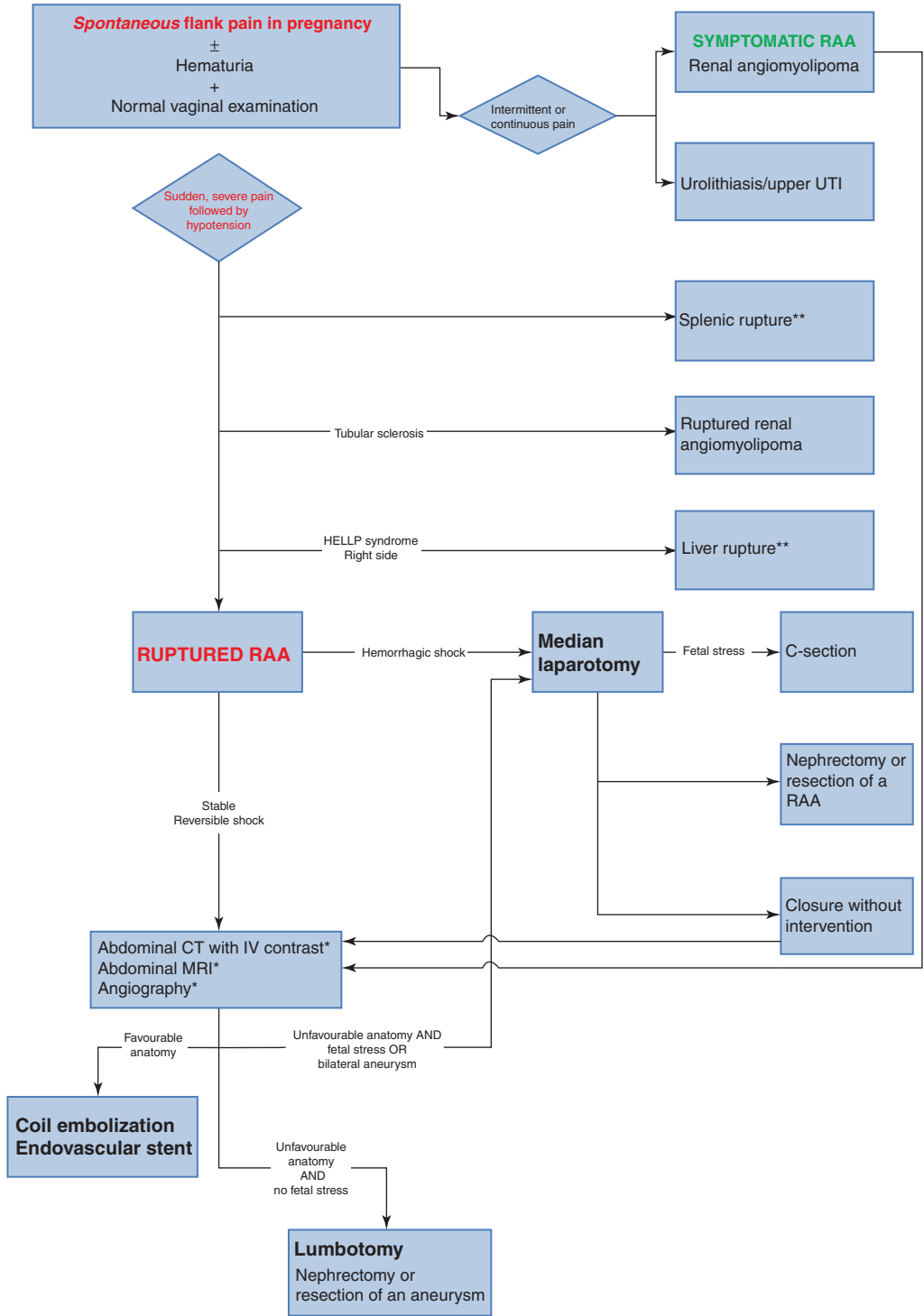
A complete diagnostic-therapeutic algorithm for RAA in pregnancy is presented in Fig. 29.8.



**Fig. 29.7** (a, b) The RAA in the right renal hilum. Red vessel loops were placed proximally and distally to the RAA around the right renal artery. (c) The dissection of the

RAA shows a saccular form. (d) Right renal artery after primary repair of the RAA. RAA, renal artery aneurysm. (Reproduced with permission from [15] under CC BY 4.0)





**Fig. 29.8** Proposed diagnostic and treatment algorithm for suspected RAA rupture in pregnancy. \* define the type and dimensions of retroperitoneal hematoma with CT or MRI. The status of the contralateral kidney and renal artery should be defined. \*\* rarely do these patients present

with isolated flank pain. Mostly these patients have abdominal pain located on the affected side. RAA renal artery aneurysm, UTI urinary tract infection, CT, computed tomography; MRI, magnetic resonance imaging. (Reproduced with permission from [8])



#### 29.2.6.4 Obstetric Management

Indications for emergent CS are obstetric. Due to rapidly increasing severe maternal pain and sudden fetal distress, uterine rupture or placental abruption should be excluded [30].

#### 29.2.7 Prognosis

##### 29.2.7.1 Maternal Outcome

Up to 1956, maternal mortality of ruptured RAA was 100%; from 1957 to 1981, it declined to 50%; from 1982 to 2017, it further declined to 5% [8]. From 1926 to 1997, the general population's survival rate of surgically treated ruptured RAA was 74.4% (29/39) [11]. All deaths were during pregnancy. Currently, nongestational mortality is <10% [7].

##### 29.2.7.2 Fetal Outcome

Until 1956, fetal mortality of ruptured RAA was 75%; from 1957 to 1981, it declined to 62.5%; from 1982 to 2017, it further declined to 37.8% [8]. These differences are not statistically significant despite a continuous decline due to fewer patients [8]. The explanation could be that fetal death from maternal hemorrhage develops early after the onset of RAA rupture before any resuscitation or bleeding control procedures can be performed.

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### 29.3 Ruptured Renal Angiomyolipoma

#### 29.3.1 Historical Perspective

Carl August Wunderlich, in 1856, described a rare and life-threatening condition characterized by nontraumatic renal bleeding into the subcapsular

and perinephric space [39]. Paul Albert Grawitz first described angiomyolipoma in 1900 [40].

#### 29.3.2 Incidence

The incidence is 0.13% in the general population, represents 3% of solid renal masses, and is even more infrequent during pregnancy [41, 42]. Less than 50 cases have been described in pregnancy [43]. Interestingly, 13% of these patients had tuberous sclerosis [43].

#### 29.3.3 Pathophysiology

Renal angiomyolipoma (RAML) is often a benign tumor consisting of adipocytes, smooth muscle cells, and blood vessels with a thickened wall. In the general population, immunological mechanisms could be influential, and there is an increased number of estrogen and progesterone receptors at the muscle cell level [44]. Positive receptors for estrogen and progesterone have been found in more than 25% of cases [45]. Hormonal influence is further confirmed by (1) autopsy—the incidence of RAML is 1/330 women compared to 1/5000 men [46], (2) growth during pregnancy [47], and (3) accelerated growth during ovarian stimulation therapy [48]. All RAMLs in patients with TS expressed the aromatase receptor in the general population. The mean age of presentation in pregnancy is 31 years, lower than 43 years in the general population [49]. The tumors from patients with TS were significantly more likely to express both ER $\alpha$  and progesterone receptors than sporadic RAML [50].

During pregnancy, the risk of spontaneous rupture is higher due to accelerated growth due to hormonal influence, increasing abdominal pres-

sure, and blood volume [49, 51]. Therefore, ruptured RAML is one presentation of Wunderlich's syndrome (nontraumatic renal bleeding into the subcapsular and perinephric space) [52]. Important findings are [43, 53]:

- The average tumor size is 10 cm,
- The tumor size does not correlate with the risk of rupture,
- 81% rupture during pregnancy.

### 29.3.4 Clinical Presentation

Symptoms depend on whether RAML has ruptured. Unruptured RAML presents as an asymptomatic or slightly painful lumbar palpable mass. With rupture, the pain intensifies, or sudden onset of severe flank pain ensues [52]. Further presentation depends on the severity of retroperitoneal bleeding (see Sect. 29.2.3). Macrohematuria is common.

### 29.3.5 Differential Diagnosis

See Sect. 29.2.4.

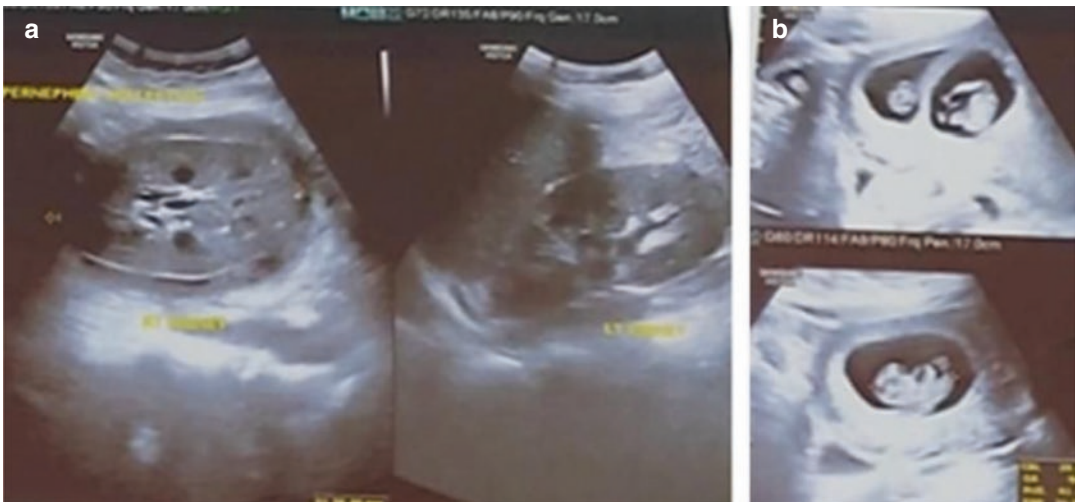
### 29.3.6 Diagnosis

#### 29.3.6.1 Laboratory Findings

Laboratory tests used are similar to ruptured RAA (see Sect. 29.2.5.1), although, due to a lesser degree of bleeding and hemorrhagic shock, almost all patients have an initial complete blood count. With smaller bleeding, initial Hgb values can be normal [52]. WBC levels are often elevated [52].

#### 29.3.6.2 Transabdominal Ultrasound

The US findings of rupture and hemorrhage of RAML show a strong, lamellar heterogeneous echogenic mass [42], similar to *onion skin* in the kidney area when it occurs under the renal capsule (Fig. 29.9). It should be distinguished from the nonbleeding hamartomas, which can appear mixed. If the tumor ruptures and bleeds out of the renal capsule, there is an echoless stripe zone around the hematoma, and the no-echo area may be more reliable for diagnosing the rupture. The Color Doppler US can measure the blood flow of the RAML [55] and exclude an aneurysm. Abdominal CT or MRI confirms the diagnosis if needed.

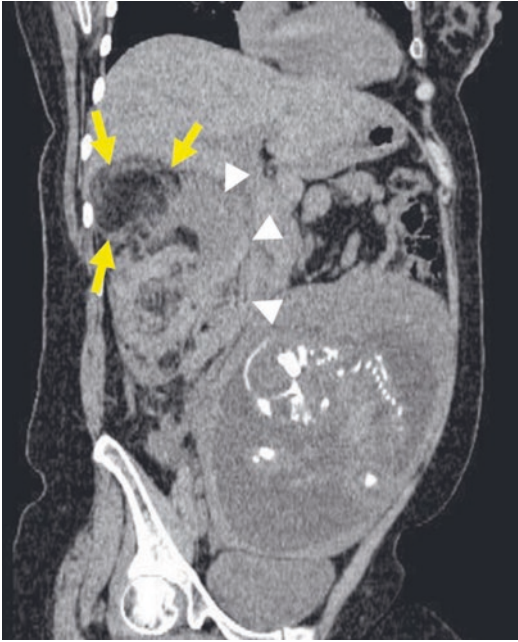


**Fig. 29.9** (a) Renal US of ruptured renal angiomyolipoma shows a multiple hyperechoic lesion in the upper pole of the right kidney with surrounding hematoma. (b)

Live twin pregnancy at 11 weeks. (Reproduced with permission from [54] under the CC BY 4.0 Attribution License)

### 29.3.6.3 Abdominal CT

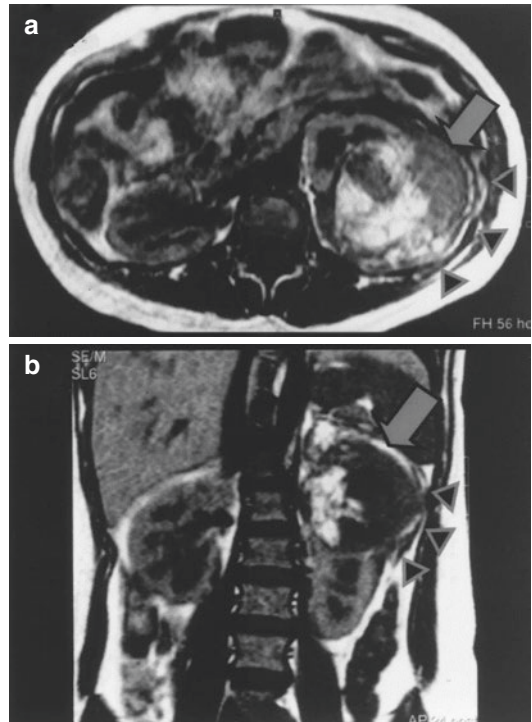
Nonruptured and ruptured (retroperitoneal hematoma) RAML is suspected on native abdominal CT when a component with a density of fatty tissue is found (Fig. 29.10). Abdominal lymphadenopathy is not characteristic [56].



**Fig. 29.10** Abdominal CT shows a right renal tumor (yellow arrows) of 8 cm containing a fat component with retroperitoneal hematoma (arrowheads). (Reproduced with permission from [43])

### 29.3.6.4 Abdominal MR/MR Urography

Abdominal MR or MR urography delineates adjacent parenchymal structures and defines underlying pathology in cases of ruptured RAML (Fig. 29.11).



**Fig. 29.11** T1-weighted MR shows a ruptured angiomyolipoma (arrow) of the left kidney with retroperitoneal hemorrhage (arrowheads) at 27 weeks gestation. (a) axial, (b) coronal. (Reproduced with permission from [57])

### 29.3.7 Treatment

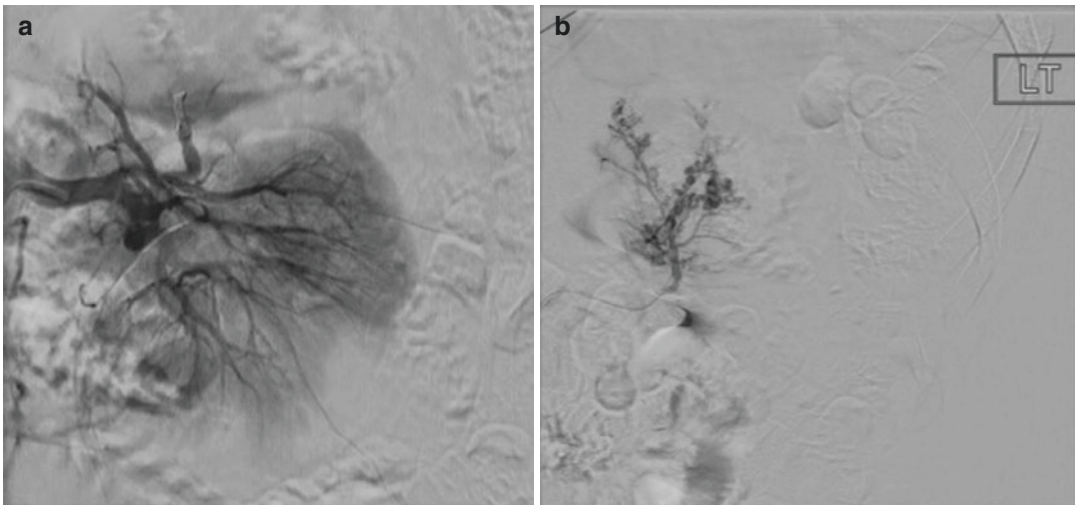
#### 29.3.7.1 Conservative Treatment

Conservative treatment during pregnancy is possible if the mother and fetus are hemodynamically stable. It includes bed rest and iron supplementation [57]. Successful conservative treatment was completed in 31% [43]. Close monitoring and emergency response for rerupture are required [58], which occurred in 14% of conservatively treated patients [43]. Since the average gestational age for rupture is 26–28 weeks [43, 53], fetal immaturity is the issue. Conservative management should be carried out before the 32nd week in hemodynamically stable patients. However, some prefer to finalize gestation at the 28th week after fetal lung maturation,

treating the RAML during the same surgery [59, 60]. After delivery, percutaneous transcatheter arterial embolization is the preferred treatment.

#### 29.3.7.2 Percutaneous Embolization

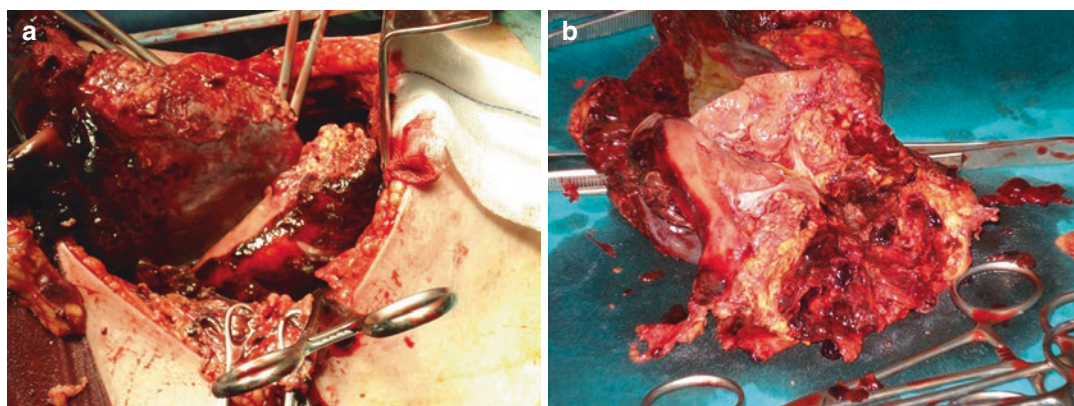
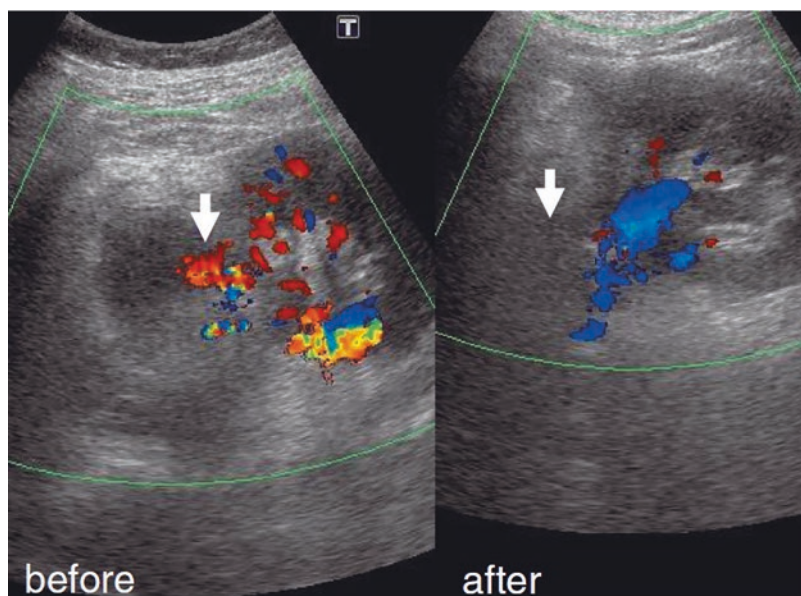
For RAML in patients with tuberous sclerosis, which tends to grow rapidly [61, 62], RAML >4 cm [52, 55, 56], or symptomatic or bleeding RAML [52], transarterial embolization (Fig. 29.12) is preferred over observation. The treatment efficacy is confirmed immediately by (low pulse) angiography. Color Doppler US confirms the decrease of tumor blood flow (Fig. 29.13) and minimizes total radiation exposure replacing the confirmation angiography. Weekly clinical and US follow-up is mandatory [52].



**Fig. 29.12** Interventional radiology fluoroscopy of left renal angiomyolipoma, (a) before and (b) after the embolization. (Reproduced with permission from [52])



**Fig. 29.13** Color Doppler sonography before and after transarterial embolization shows no blood flow in the tumor (arrows). (Reproduced with permission from [43])



**Fig. 29.14** (a) Ruptured renal angiomyolipoma during nephrectomy. (b) Nephrectomy specimen shows angiomyolipoma with hemorrhagic foci [42]

### 29.3.7.3 Surgical Treatment

An absolute indication for emergent exploration is maternal hemodynamic instability. Previously, the treatment was nephrectomy (Fig. 29.14) [63]. However, a partial nephrectomy is possible in selected cases [64]. The preoperative status of the contralateral kidney determines (1) additional attempts for kidney salvage, (2) interventional, nonoperative management, and (3) immediate

postoperative dialysis if both kidneys are absent or afunctional. Growing RAML could be removed at the optimal time during the second trimester. Nonruptured RAML during the third trimester should be monitored and operated on only in hemodynamically unstable patients when (partial) nephrectomy is performed simultaneously with CS [65] or after delivery. In the last scenario, a laparoscopic approach is feasible [53].



Approximately 54% of pregnant patients underwent nephrectomy, whereas 46% were treated conservatively with or without arterial embolization [53].

### 29.3.7.4 Obstetric Management

Maternal hemodynamic instability due to the ruptured RAML increases the rate of emergent CS up to 56% [43, 53]. Term vaginal delivery with unruptured [53] or antepartum-ruptured RAML with hemodynamic stability [52, 57] is successful under strict maternal and fetal monitoring. There is no evidence that the incidence of RAML rupture during vaginal delivery is higher than during CS. Vacuum extraction can also be an alternative to shorten the second stage of the labor, or induced vaginal delivery at 36–37 weeks is feasible [53].

## 29.3.8 Prognosis

### 29.3.8.1 Maternal Outcome

Percutaneous transarterial embolization shortens hospitalization compared to surgical treatment [52, 55, 56]. Embolization of large RAML can result in renal abscess treated by percutaneous drainage [62].

### 29.3.8.2 Fetal Outcome

The fetal outcome depends on maternal hemodynamic stability. Maternal hemodynamic instability carries fetal mortality of 30%, while maternal hemodynamic stability leads to fetal survival of 100% (Table 29.2) [52]. The risk of malformation is high with a fetus <10 weeks old, and the cancer risk to the fetus increases due to radiation exposure from embolization [62].

**Table 29.2** Fetal prognosis according to maternal hemodynamic stability at the time of renal angiomyolipoma rupture

| Stability | <i>n</i> | Term delivery | Urgent CS | Fetal death | Unclear |
|-----------|----------|---------------|-----------|-------------|---------|
| Stable    | 22       | 20 (91%)      | 0 (0%)    | 0 (0%)      | 2 (9%)  |
| Unstable  | 20       | 2 (10%)       | 9 (45%)   | 6 (30%)     | 3 (15%) |
| Unclear   | 3        | –             | –         | –           | –       |

Reproduced with permission from [43]

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